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HIGH PRODUCTION VOLUME (HPV)

CHALLENGE PROGRAM

TEST PLAN

For

PETROLEUM ADDITIVE ALKARYL SULFONATE CATEGORY

Prepared by

**The American Chemistry Council
Petroleum Additives Panel
Health, Environmental, and Regulatory Task Group**

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List of Member Companies in the Health, Environmental, and Regulatory Task Group

The Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council Petroleum Additives Panel includes the following member companies:

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Crompton Corporation

Ethyl Corporation

ExxonMobil Chemical Company

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EXECUTIVE SUMMARY

The American Chemistry Council Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG), and its member companies, hereby submit for review and public comment its test plan for the “*petroleum additive alkaryl sulfonate*” category of chemicals under the Environmental Protection Agency’s High Production Volume (HPV) Challenge Program. This report should be read in its entirety in order to obtain an understanding of the category and proposed testing.

Alkaryl Sulfonate Category. Based on several factors specified in EPA’s guidance document on “Development of Chemical Categories in the HPV Challenge Program,” in which use of chemical categories is encouraged, the following twelve closely related chemicals constitute a chemical category:

- sulfonic acids, petroleum, calcium salts - (CAS # 61789-86-4, referred to in this report as petroleum derived calcium salt)
- sulfonic acids, petroleum, barium salts - (CAS # 61790-48-5, referred to in this report as petroleum derived barium salt)
- sulfonic acids, petroleum, sodium salts - (CAS # 68608-26-4, referred to in this report as petroleum derived sodium salt)
- sulfonic acids, petroleum, calcium salts, overbased - (CAS # 68783-96-0, referred to in this report as petroleum derived calcium salt, overbased)
- benzenesulfonic acid, mono-C16-C24 alkyl derivatives, calcium salts - (CAS # 70024-69-0, referred to in this report as C 16-C24 alkaryl calcium salt derivative)
- benzenesulfonic acid, mono-C 15-C30 branched alkyl and di-C 11 -C 13 branched and linear alkyl derivatives, calcium salts, overbased - (CAS # 71486-79-8, referred to in this report as mixed mono-C 1 5-C30 and di-C 11 -C 13 alkaryl calcium salt, overbased derivative)
- benzenesulfonic acid, mono-C 15-C30 branched alkyl and di-C 11 -C 13 branched and linear alkyl derivatives - (CAS # 71549-79-6, referred to in this report as mixed **mono-C 15X30** and di-C 11 -C 13 alkaryl derivative)
- ⌘ benzenesulfonic acid, mono and dialkyl derivatives, magnesium salts - (CAS # 71786-47-5, referred to in this report as alkaryl magnesium salt derivative)
- benzenesulfonic acid, C 15-C30 alkyl derivatives, sodium salts - (CAS # 78330-12-8, referred to in this report as C15-C30 alkaryl sodium salt derivative)
- benzenesulfonic acid, C 14-C24 branched and linear alkyl derivatives, calcium salts - (CAS # 115733-09-0, referred to in this report as C14-C24 alkaryl calcium salt derivative)
- ⌘ benzenesulfonic acid, C 14-C24 branched and linear alkyl derivatives, calcium salts, overbased - (CAS # 115733-10-3, referred to in this report as C14-C24 alkaryl calcium salt, overbased derivative)
- ⌘ benzenesulfonic acid, C14-C24 branched and linear alkyl derivatives - (CAS # 115829-36-2, referred to in this report as C14-C24 alkaryl derivative)

Structural Similarity. A key factor supporting the classification of these chemicals as a category is their structural similarity. All substances in this category consist of a benzene ring with a sulfonic acid substituent group and one or more long-chain alkyl substituent groups that vary in length and extent of branching. Most of these substances have been neutralized by an alkali metal base to form the corresponding alkali metal salt.

Similarity of Physicochemical Properties. The similarity of the *physicochemical properties* of these substances parallels their structural similarity. All are dark colored viscous liquids intended for use as components in finished lubricating oils. The use of these substances in finished lubricants requires that they be stable under high temperatures (>100°C). Their low volatility is due to their low vapor pressure, high viscosity, and relatively high molecular weights. The existing information for these substances indicates that they have low water solubility. However, additional water solubility data will be collected.

Fate and Transport Characteristics. Members of this category have been shown to be poorly biodegradable. However, additional biodegradation testing will be conducted to determine whether there is potential for a higher degree of biodegradability for members of this category that have linear alkyl groups. Since the members of this category have low water solubility, hydrolysis testing is technically unfeasible. Furthermore, members of the category are resistant to hydrolysis because they lack hydrolyzable moieties. This makes hydrolysis modeling unnecessary. Photodegradation is not expected to cause significant physical degradation of petroleum additive alkaryl sulfonates. However, computer-modeled data will be developed to adequately characterize the potential atmospheric oxidation potential for members of this category. Although these substances are not expected to partition to water or air if released into the environment due to their low water solubility and low vapor pressure, computer-modeled environmental partitioning data will be calculated on the members of this category.

Toxicological Similarity. Review of existing published and unpublished test data for petroleum additive alkaryl sulfonates shows the *aquatic and mammalian toxicity* among the twelve substances within this category are similar and are of a low concern.

Aquatic Toxicology. Data on acute fish toxicity, acute invertebrate toxicity, and alga toxicity were reviewed, and the findings indicate little to no toxicity to fish, aquatic invertebrates, and alga when appropriate test methods are used. However, additional tests will be conducted so that this category may be adequately characterized for aquatic toxicity.

Mammalian Toxicology - Acute. Data on acute mammalian toxicity were reviewed, and the findings indicate a low concern for acute toxicity. Data are available for most members of the category indicating that the category has been well tested for acute mammalian effects. Therefore, no additional acute mammalian toxicity testing is necessary.

Mammalian Toxicology - Mutagenicity. Data from bacteria 1 reverse mutation assays and *in vitro* and *in vivo* chromosome aberration studies were reviewed, and the findings indicate a low concern for mutagenicity. Data are available for several members of the category or structural analogs, and these data can be bridged to the other members of the category. Therefore, the

category has been adequately tested for mutagenicity, and no additional mutagenicity testing is necessary.

Mammalian Toxicology • Subchronic Toxicity. Data from repeated-dose toxicity studies were reviewed. Minimal signs of toxicity were observed following repeated oral exposure. Adverse effects at the site of contact were observed following repeated dermal exposure (injury to the skin) and repeated inhalation (injury to the lungs). These findings can be bridged to the remaining members of the category. However, an additional repeated-dose toxicity study will be conducted as a dossetting study for the reproductive toxicity described below.

Mammalian Toxicology • Reproductive and Developmental Toxicity. There are no published or unpublished reproductive/developmental studies for members of the petroleum additive alkaryl sulfonate category. A one-generation reproductive toxicity test will be conducted to provide data that can be bridged to the remainder of the category.

Conclusion. Based upon the data reviewed in the report, the physicochemical and toxicological properties of the proposed petroleum additive alkaryl sulfonate category members are similar and follow a regular pattern as a result of that structural similarity. Therefore, the EPA definition of a chemical category has been met, and the twelve chemicals that constitute the petroleum additive alkaryl sulfonate category will be tested in accordance with the test plan summarized below.

Test Plan. The test plan for the petroleum additive alkaryl sulfonate category includes the following tests and computer modeling:

- Water solubility – Petroleum derived calcium salt (CAS # 61789-86-4), petroleum derived barium salt (CAS # 61790-48-5), petroleum derived sodium salt (CAS # 68608-26-4), C15-C30 alkaryl sodium salt (CAS # 78330-12-8), and C14-C24 alkaryl calcium salt derivative (CAS # 115733-09-0) will be tested.
- Biodegradability – C 15-C30 alkaryl sodium salt (CAS # 78330-12-8) will be tested.
- Photodegradation (atmospheric oxidation) modeling – Data will be developed using the AOP model in EPIWIN.
- Fugacity modeling – Environmental partitioning data will be calculated using a Mackay Level I equilibrium partitioning model.
- Acute fish toxicity • Limit tests will be conducted on petroleum derived barium salt (CAS # 61790-48-Q petroleum derived sodium salt (CAS # 68608-26-4), petroleum derived calcium salt (CAS # 61789-86-4), and C14-C24 alkaryl calcium salt derivative (CAS # 115733-09-o).
- Acute invertebrate toxicity - Limit tests will be conducted on petroleum derived sodium salt (CAS # 68608-26-4) and petroleum derived calcium salt (CAS # 61789-86-4).
- Alga toxicity • Limit tests will be conducted on petroleum derived sodium salt (CAS # 68608-26-4) and petroleum derived calcium salt (CAS # 61789-86-4).
- Repeated-dose toxicity • C14-C24 alkaryl calcium salt derivative (CAS # 115733-09-o) will be tested in a 28-day dose-range finding study for the reproductive/developmental toxicity study.
- Reproductive/developmental toxicity • C 14-C24 alkaryl calcium salt derivative (CAS # 115733-09-o) will be tested in a one-generation study.

As this test plan was developed, careful consideration was given to the number of animals that would be required for tests included in the proposed plan and conditions to which the animals might be exposed. In consideration of the concerns of some non governmental organizations about animal welfare, the use of animals in this proposed test plan has been minimized.

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1.0 INTRODUCTION

In March 1999, the American Chemistry Council (formerly the Chemical Manufacturers Association) Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG), and its participating member companies committed to address data needs for certain chemicals listed under the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program. This test plan follows up on that commitment.

Specifically, this test plan sets forth how the HERTG intends to address testing information for the twelve substances listed in Table 1 and represented structurally in Table 2. These twelve substances include:

- sulfonic acids, petroleum, calcium salts - (CAS # 61789-86-4, referred to in this report as petroleum derived calcium salt)
- sulfonic acids, petroleum, barium salts - (CAS # 61790-48-5, referred to in this report as petroleum derived barium salt)
- sulfonic acids, petroleum, sodium salts - (CAS # 68608-26-4, referred to in this report as petroleum derived sodium salt)
- sulfonic acids, petroleum, calcium salts, overbased - (CAS # 68783-96-0, referred to in this report as petroleum derived calcium salt, overbased)
- benzenesulfonic acid, mono-C16-C24 alkyl derivatives, calcium salts- (CAS # 70024-69-0, referred to in this report as C16-C24 alkaryl calcium salt derivative)
- benzenesulfonic acid, mono-C 15-C30 branched alkyl and di-C 11 -C13 branched and linear alkyl derivatives, calcium salts, overbased - (CAS # 71486-79-8, referred to in this report as mixed mono-C 15-C30 and di-C11 -C13 alkaryl calcium salt, overbased derivative)
- benzenesulfonic acid, mono-C 15-C30 branched alkyl and di-C 11 -C 13 branched and linear alkyl derivatives - (CAS # 71549-79-6, referred to in this report as mixed mono-C15-C30 and di-C11 -C13 alkaryl derivative)
- benzenesulfonic acid, mono and dialkyl derivatives, magnesium salts - (CAS # 71786-47-5, referred to in this report as alkaryl magnesium salt derivative)
- benzenesulfonic acid, C15-C30 alkyl derivatives, sodium salts - (CAS # 78330-12-8, referred to in this report as C15-C30 alkaryl sodium salt derivative)
- benzenesulfonic acid, C 14-C24 branched and linear alkyl derivatives, calcium salts - (CAS # 115733-09-0, referred to in this report as C14-C24 alkaryl calcium salt derivative)
- benzenesulfonic acid, C 14-C24 branched and linear alkyl derivatives, calcium salts, overbased - (CAS # 115733-10-3, referred to in this report as C14-C24 alkaryl calcium salt, overbased derivative)
- benzenesulfonic acid, C 14-C24 branched and linear alkyl derivatives - (CAS # 115829-36-2, referred to in this report as C14-C24 alkaryl derivative)

An analysis of the available data on these chemicals supports the designation of the petroleum additive alkaryl sulfonates as a “chemical category” as provided in the EPA guidance document entitled, “Development of Chemical Categories in the HPV

Challenge Program.” This document provides the basis for that determination, indicates the findings of the data review process, and sets forth a proposed test plan to satisfy parts of the required test battery for endpoints without data that would be considered adequate under the program.

EPA guidance on the HPV Challenge Program indicates that the primary purpose of the program is to encourage “the chemical industry . . . to voluntarily compile a Screening Information Data Set (SIDS) on all chemicals on the US HPV list.” (EPA, “Development of Chemical Categories in the HPV Challenge Program,” p. 1) At the same time, EPA recognizes that the “large number of chemicals to be tested [about 2800 HPV chemicals] makes it important to reduce the number of tests to be conducted, where *this is scientifically justifiable*.” (Id., p. 1) [emphasis added]. The next part of the guidance explains where this would be scientifically justifiable:

One approach is to test closely related chemicals as a group, or category, rather than test them as individual chemicals. In the category approach, not every *chemical needs to be tested for every SIDS endpoint*. However, *the test data finally compiled* for the category must prove adequate to support a screening level hazard-assessment of the category and its members. That is, the *final data set* must allow one to estimate the hazard for the untested endpoints, *ideally* by interpolation between and among the category members. In certain cases, where toxicity is low and no upward trend is expected, extrapolation to the higher category members may be acceptable. (Id., p. 1) [emphasis added].

EPA guidance goes on to state, “The use of categories is encouraged in the Challenge Program and will have a number of benefits.” (Id., p. 1) Among the benefits identified in the guidance for the use of categories are “a reduction in testing will result in fewer animals used to test a category of chemicals as opposed to doing each test on each individual chemical,” and “there will be . . . economic savings since less testing may be needed for chemicals considered as a category.” (Id., p. 1) That guidance also states that categories “accomplish the goal of the Challenge Program – to obtain screening level hazard information – through the strategic application of testing to the category.” (Id, p. 2)

A similarly stated intent “to reduce the number of tests to be conducted, *where this is scientifically justifiable*” was articulated by the Agency in its draft guidance document titled, “The Use of Structure Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program.” [emphasis added].

The EPA “Chemical Categories” guidance sets forth a definition of what constitutes a “chemical category, for the purposes of the Challenge Program.” Specifically, that definition states that a chemical category under the HPV Challenge Program “is a group of chemicals whose physicochemical and toxicological properties *are likely to be similar or follow a regular pattern as a result of structural similarity*.” (Op. Cit., p. 2) [emphasis added].

According to the guidance, what is important is that the “structural similarities [among members of the group] *may* create a predictable pattern in any or all of the following parameters: physicochemical properties, environmental fate and effects, and human health effects.” (Id., p. 2) [emphasis added]. Thus, it is not necessary for the chemicals in a category to be similar in all respects. Nor must there be conclusive proof that the chemicals in the postulated category will behave identically across all relevant parameters. All that is required for an acceptable category under the HPV Challenge Program is that there be a *likelihood* of similarity of physicochemical and toxicological properties or a *likelihood* that the chemicals will in some pertinent respect follow a regular pattern as a result of their structural similarity.

In identifying the petroleum additive alkaryl sulfonate category, the six-step process set out in the EPA guidance on category development was followed. As the information below indicates, the petroleum additive alkaryl sulfonate category of chemicals clearly satisfies the standards established in that guidance for use of a chemical category:

Step 1: group structurally similar chemicals into a putative category

Step 2: gather relevant published and unpublished literature for each member of the category

Step 3: evaluate the compiled data for adequacy in accordance with the EPA guidance documentation

Step 4: construct matrices of SIDS endpoints versus category members arranged so as to indicate the structural progression of the category (in this case, by increasing alkyl side chain length in Tables 3-9)

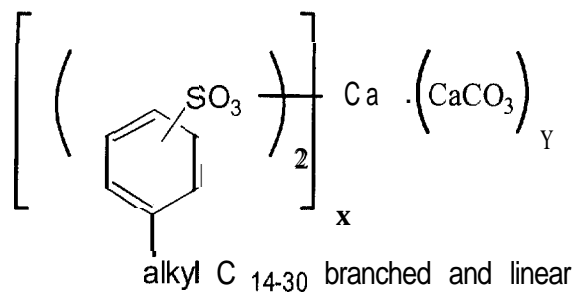
Step 5: evaluate the data to determine whether there is a correlation between category members for each SIDS endpoint

Step 6: make available to EPA, and to the public for review, this test plan including the foregoing category definition and rationale and the following data assessment with the proposed testing scheme for the petroleum additive alkaryl sulfonates.

2.0 CHEMICAL DESCRIPTION OF ALKYL SULFIDE CATEGORY

2.1 DESCRIPTION

Alkaryl sulfonates consist of a benzene ring with a sulfonic acid substituent group and one or more long-chain alkyl substituent groups. The alkyl groups are saturated hydrocarbon chains that vary in length and extent of branching. A basic metal may neutralize the acid group, and calcium is typically used. A general structure is shown below.



As a general class, these substances are commonly used as detergents and surface-active agents by many industries. However, subclasses of alkaryl sulfonates exist with somewhat different physical and chemical properties based on the performance requirements of the various industries. For example, the consumer detergent industry tends to use alkaryl sulfonates with alkyl groups of 12 carbons or less to support miscibility in water.

The alkaryl sulfonates that are the subject of this test plan are used as petroleum additives in petroleum base stocks. The chemical names and CAS numbers for the members of the petroleum additive alkaryl sulfonate category are presented in Table 1. The chemical structures for the members of the category are presented in Table 2. These substances are prepared by sulfonation of either synthetic alkylbenzene substrates or naturally occurring alkylaromatic-rich fractions of heavy lubricating oil base stocks derived from petroleum streams. The alkyl substituent group may vary in number (e.g., mono- or dialkyl), position (e.g., predominantly meta or para to the sulfonic acid position), chain length (e.g., C14 to C30) or in the degree of branching. The distribution of the alkyl chain lengths for several members of the category are presented in Figure 1. Branched and linear alkyl groups of 20 or more carbons are used to enhance oil solubility. Although branched alkyl groups are generally presumed to be more water-soluble than straight chains, petroleum additive alkaryl sulfonates have such low water solubility that the degree of branching does not affect their solubility and performance in petroleum base stocks.

The petroleum additive alkaryl sulfonates are manufactured in petroleum base stocks, and thus the substrates are never isolated. The sulfonic acid substituent group can be neutralized by alkali metal bases to form the corresponding alkali metal salt. For the members of the petroleum additive alkaryl sulfonate category, the sulfonic acid substituent group may be present as the free acid or as a salt of sodium, calcium, magnesium or barium. The salts can also be complexed ("overbased") with an excess of metal carbonate. The overbased products are produced in the presence of the alkaryl sulfonic acid salt (soap) by adding excess metal hydroxide and carbon dioxide. The over basing reaction forms the metal carbonate which exists in the lubricating oil diluent as a reverse micelle (i.e., the metal carbonate is in the center of the micelle with the alkaryl sulfonic acid salt [soap] surrounding the carbonate). Figure 2 shows the general structure of a petroleum additive alkaryl sulfonate reverse micelle. The ratio of metal carbonate to soap can range from a low of 6: 1 to a high of 30: 1. As the ratio increases, the alkaryl

sulfonic acid salt (soap) content is diluted. Thus, the overbased members of the category are considered more dilute analogs of the category members that are not overbased.

2.2 PHYSICOCHEMICAL PROPERTIES

The physicochemical properties of the members of the petroleum additive alkaryl sulfonate category are presented in Table 3. They are all dark colored viscous liquids at ambient temperature. The similarities in the other physicochemical properties of these substances, which are described below, are explained by similarities in their chemical structure and processing and provide justification of this group of chemicals as a category within the HPV Challenge Program.

2.1.1 Molecular Weight and Alkyl Side Chain Length

The members of the category range in molecular weight from 354 to 1194 daltons. However, these substances will dissociate to some degree in aquatic environments and biological systems, and it is better to characterize the members by their equivalent weight to evaluate their toxicity. The equivalent weight is the weight of one alkylbenzene sulfonic acid plus the weight of the alkali metal.

Two structural variables in the category influence the variability in equivalent weight of the category members: the alkali metal and the alkyl side chain length. The latter also has an influence on water solubility and the ability of the member of the category to cross biological membranes, which in turn influences bioavailability. The carbon chain length range for each member of the category is presented in Table 3, and the fractional distribution of each carbon number is illustrated in Figure 1 for several members of the category. Due to the influence of carbon chain length on bioavailability, the members of the category are arrayed in order of increasing carbon chain length in Tables 3-9.

2.1.2 Specific Gravity

Available specific gravity data are presented in Table 3. The specific gravity of the overbased members of the category is approximately 1.1. The specific gravity of the category members that are not overbased is slightly less than 1.0.

2.1.3 Viscosity

Available viscosity data are presented in Table 3. As manufactured in petroleum base stocks, the viscosity of the members of the petroleum additive alkaryl sulfonate category is approximately 200 cSt @ 100°C (Table 3) and 1500 cSt @ 40°C.

2.1.4 Melting Point

The high viscosity of the members of the category makes it technically unfeasible to determine their melting point. However, modeling data indicates that the melting point of the “de-oiled” substances ranges from 208°C to 350°C (Table 3).

2.1.5 Boiling Point

The use of these substances in finished lubricants requires that they be thermally and chemically stable under high temperatures (>100°C). Typically, the petroleum base stocks in these substances boil at temperatures above 300°C. Modeling data indicates that the boiling point of the “de-oiled” substances ranges from 506°C to 936°C (Table 3).

2.1.6 Vapor Pressure

Since “de-oiled” petroleum additive alkaryl sulfonates are solid, their vapor pressure can be estimated from the vapor pressure of the petroleum base stocks in which they are manufactured. Typically, these base oil stocks have low vapor pressure, < 10⁻¹⁰ Pa @ 25°C (Table 3). Thus, the low volatility of the members of the petroleum additive alkaryl sulfonates is due to their low vapor pressure, high viscosity, and high relative molecular weights.

2.1.7 Water Solubility and Octanol-Water Partition Coefficients

Data for mixed mono-Cl 5-C30 and di-Cl 1-C13 alkaryl derivative (CAS # 71549-79-6) and a C20-C24 alkaryl calcium salt derivative (no CAS #) analog of C16-C24 alkaryl calcium salt derivative (CAS # 70024-69-0) indicate that these substances have low water solubility, < 1ppm (Table 3). The log of the octanol-water partition coefficients of these substances is greater than 6.0 (Table 3).

The low water solubility of these two substances is consistent with the presence of the long hydrocarbon side chain. However, additional water solubility data will be determined for one substance that contains a shorter alkyl side chain, C 14-C24 alkaryl calcium salt derivative (CAS # 115733-09-0), and two substances that are sodium salts, petroleum derived sodium salt (CAS # 6860-26-4), C15-C30 alkaryl sodium salt derivative (CAS # 78330-12-g). Water solubility will also be determined on two additional substances to support their acute aquatic toxicity evaluation, petroleum derived calcium salt (CAS # 6 1789-86-4) and petroleum derived barium salt (CAS 6 1790-48-5).

3.0 USES OF PETROLEUM ADDITIVE ALKARYL SULFONATES

Petroleum additive alkaryl sulfonates are used to formulate finished lubricating oils including all types of automotive and diesel engine crankcase oils, air and water-cooled two-cycle engine oils, industrial oils, hydraulic fluids, gear oils, and metal working lubricating oils. They are used as high temperature detergents to reduce deposits on

pistons, engine crankcases, and hydraulic equipment parts and as rust inhibitors during industrial oil use. Petroleum additive alkaryl sulfonates are generally sold to finished oil blenders in additive packages, where the concentration ranges from 1 to 50 wt.%. These additive packages are then blended into finished oils where the typical concentration of alkaryl sulfonate ranges from 0.1 to 10 wt.% in the finished oil.

Petroleum additive alkaryl sulfonates are manufactured and blended into additive packages at plants owned by members of the HERTG. Finished lubricants are blended at facilities owned by our customers. Additive packages are shipped to customers in bulk in ships, isocontainers, railroad tank cars, tank trucks or in **55-gallon** steel drums. The bulk additive packages are stored in bulk storage tanks at the customer blending sites. Finished oils are blended by pumping the lubricating oil blend stocks and the additive package from their storage tanks through computer controlled valves that meter the precise delivery of the components into a blending tank. After blending, the finished lubricant products are sold in bulk and shipped in tank trucks to large industrial users, such as manufacturing facilities and facilities that service truck fleets and passenger motor vehicles. Finished lubricants are also packaged into **55-gallon** drums, **5-gallon** pails, and one-gallon and one-quart containers for sale to smaller industrial users. Sales of lubricants in one-gallon and one-quart containers to consumers at service stations or retail specialty stores also occur.

Based on these uses, the potentially exposed populations include (1) workers involved in the manufacture of alkaryl sulfonates, blending them into additive packages, and blending the additive packages into finished lubricants; (2) quality assurance workers who sample and analyze these products to ensure that they meet specifications; (3) workers involved in the transfer and transport of alkaryl sulfonates, additive packages or finished lubricants that contain them; (4) mechanics who may come into contact with both fresh and used lubricants while working on engines or equipment; (5) gasoline station attendants and consumers who may periodically add lubricating oil to automotive crankcases; and (6) consumers who may change their own automotive engine oil. The most likely route of exposure for these substances is skin and eye contact. Manufacturing, quality assurance, and transportation workers will likely have access to engineering controls and wear protective clothing to eliminate exposure. Mechanics wear protective clothing, but often work without gloves or eye protection. Gasoline station attendants and consumers often work without gloves or other protective equipment. The most likely source of environmental exposure is accidental spills at manufacturing sites and during transport.

4.0 EVALUATION OF AVAILABLE PUBLIC AND COMPANY DATA

4.1 ENVIRONMENTAL FATE DATA

4.1.1 Physicochemical Properties Relevant to Environmental Fate

In order to understand the environmental fate of a substance, one must understand how that substance and its degradation by-products partition among environmental compartments (i.e., air, soil, sediment, suspended sediment, water, and biota). The

physicochemical properties of a substance influence the way in which a substance will degrade. The important environmental degradation pathways are biodegradation, hydrolysis, and photodegradation. Biodegradation is a measure of the potential of compounds to be degraded by microorganisms. Hydrolysis is a reaction in which a water molecule or hydroxide ion substitutes for another atom or group of atoms present in an organic molecule. Photodegradation is the degradation of a chemical compound as a result of absorption of solar radiation.

The physicochemical properties of the parent substance and its degradation by-products will also influence the way in which these substances will partition among environmental compartments. Substances characterized by a low vapor pressure do not partition into air to any great extent. Similarly, substances that are characterized by low water solubility do not partition extensively into water. Substances that do not partition into air and water to any great extent tend to partition into soil and sediments.

4.1.2 Biodegradability

4.1.2.1 Test Methodologies

Chemical biodegradation involves a series of microbially-mediated reactions that may require many kinds of microorganisms acting together to degrade the parent substance. There are several standard test methods, which measure primary degradation (i.e., loss of parent chemical) or ultimate degradation (i.e., complete utilization of the substance to produce carbon dioxide, water, mineral salts, and microbial biomass). Primary degradation can be determined analytically by measuring dissolved organic carbon (DOC) for water-soluble chemicals, infrared absorbance, or by a chemical-specific detection method. Ultimate degradation (also called mineralization) can be determined by measuring oxygen consumption or carbon dioxide evolution relative to the theoretical levels that can be achieved based on an elemental analysis of the chemical under investigation.

4.1.2.2 Summary of Available Data

Biodegradation data for the petroleum additive alkaryl sulfonate category is summarized in Table 4. Two members of the category and one structural analog¹ have been adequately tested.

Two substances were evaluated for biodegradability under the conditions of the *Manometric Respirometry Test* (OECD Guideline 301F). In the 28-day test for the petroleum derived calcium salt (CAS # 61789-86-4), the extent of biodegradation was 8.6% based on theoretical oxygen demand (ThOD). For the mixed mono-C15-C30 and di-C 11 -C 13 alkaryl calcium salt, overbased derivative (CAS # 71486-79-8), the extent of biodegradation in the 28-day test was 8.6% based on ThOD.

¹ An analog is an alkaryl sulfonate containing the same metal salt of the particular category member and an alkyl chain length that is within the range of the chain length of that category member.

A C20-C24 alkaryl calcium salt derivative (no CAS #) analog of the C16-C24 alkaryl calcium salt (CAS # 70024-69-0) was evaluated for biodegradability under the conditions of the *Closed Bottle Test* (OECD Guideline 301D). In the 28-day test, the extent of biodegradability was 8% based on ThOD.

4.1.2.3 Data Assessment and Test Plan for Biodegradability

In total, five biodegradation tests have been conducted on two of the twelve members of the petroleum additive alkaryl sulfonate category and three structural analogs. The alkyl side chains of these five substances are predominantly branched, and the results indicate that these substances are poorly biodegradable.

The HPV Challenge Program requires that a biodegradation test be performed or bridged to each member of a category. Adequate biodegradation data exist for two of twelve substances in the petroleum additive alkaryl sulfonate category. Additional testing and bridging will be used to fill the remaining data gaps for the other ten substances.

- A biodegradability test will be conducted on C15-C30 alkaryl sodium salt derivative (CAS # 78330-12-8), a substance that has predominantly linear alkyl side chains. The results will be bridged to C16-C24 alkaryl calcium salt derivative (CAS # 70024-69-0), which also has predominantly linear alkyl side chains and has similar physicochemical properties.
- Biodegradation data for petroleum derived calcium salt (CAS # 61789-86-4) will be bridged to the other three petroleum-derived substances in the category, which have similar chemical structures and physicochemical properties:
 - petroleum derived barium salt (CAS # 61790-48-5),
 - petroleum derived sodium salt (CAS # 68608-26-4), and
 - petroleum derived calcium salt, overbased (CAS # 68783-96-0).
- The biodegradation data for mixed mono-C15-C30 and di-C11-C13 alkaryl calcium salt, overbased derivative (CAS # 71486-79-8), which contains both branched and linear alkyl side chains, will be bridged to the other members of the category that also contain branched and linear alkyl side chains and have similar physicochemical properties:
 - mixed mono-C15-C30 and di-C11-C13 alkaryl derivative (CAS # 71549-79-6),
 - alkaryl magnesium salt derivative (CAS # 71786-47-5),
 - C14-C24 alkaryl calcium salt derivative (CAS # 115733-09-0),
 - C14-C24 alkaryl calcium salt, overbased derivative (CAS # 115733-10-3), and
 - C14-C24 alkaryl derivative (CAS # 115829-36-2).

4.1.3 Hydrolysis

4.1.3.1 Test Methodologies

The potential for a substance to hydrolyze in water is assessed as a function of pH (OECD Guideline 111, *Hydrolysis as a Function of pH*²). When an organic molecule undergoes hydrolysis, a nucleophile (water or hydroxide ion) attacks an electrophile and displaces a leaving group (e.g., halogen, phenoxide).³ Potentially hydrolyzable groups include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters⁴. The lack of a suitable leaving group renders compounds resistant to hydrolysis.

4.1.3.2 Summary of Available Data

There are no published or unpublished hydrolysis studies for members of the petroleum additive alkaryl sulfonate category. An evaluation of the hydrolytic potential of the functional groups in each substance in this category is presented in Tables 4 and 5. Substances derived from the same alkaryl sulfonic acid are grouped together in Table 5.

The twelve substances in the petroleum additive alkaryl sulfonate category do not contain functional groups that are subject to hydrolytic reactions. Desulfonation of the aromatic sulfonic acids and the corresponding salts into sulfuric acid and the aromatic hydrocarbon requires heating to 100 – 175 degrees C in dilute aqueous acid. These conditions would not be typically encountered in the environment. Thus, while the substances in the category that are salts may dissociate in water, all these substances have little, if any, potential for hydrolysis.

4.1.3.3 Data Assessment and Test Plan for Hydrolysis

Since these substances do not contain functional groups that are susceptible to hydrolytic degradative mechanisms⁴, testing these substances for hydrolysis as a function of pH is not needed to adequately evaluate this endpoint. Therefore, no hydrolysis testing is proposed for the HPV Challenge Program

4.1.4 Photodegradation

4.1.4.1 Test Methodologies

A prerequisite of photodegradation is the ability of one or more bonds of a chemical to absorb ultraviolet (UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer.

² Organization for Economic Cooperation and Development (OECD) (1993) OECD Guidelines for Testing of Chemicals. OECD. Paris, France.

³ W. Lyman et al. (1990) *Handbook of Chemical Estimation Methods*. Chapter 8.

⁴ W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt. (1982) *Handbook of Chemical Property Estimation Methods*. McGraw-Hill Book Co. New York, NY, USA.

The Atmospheric Oxidation Potential (AOP) of a substance can be characterized using the modeling program AOPWIN. This computer simulation is **recommended** in the Agency's recently released structure activity review (SAR) guidance for HPV chemicals.

4.1.4.2 Summary of Available Data

There are no published or unpublished photodegradation studies for members of the petroleum additive alkaryl sulfonate category.

None of the members of the petroleum additive alkaryl sulfonate category contain bonds that have a high potential to absorb UV light above 290 nm. These substances also have low vapor pressure, which indicates that they should not partition into the air to a significant extent.

4.1.4.3 Data Assessment and Test Plan for Photodegradation

The HPV Challenge Program requires a photodegradation test be performed or bridged to each member of a category. The Atmospheric Oxidation Potential (AOP) of these substances will be characterized using the modeling program AOPWIN. The AOP data for representative structures of the category will be evaluated to estimate (1) rate constants for the atmospheric, gas phase reaction as mediated by photochemically produced hydroxyl radicals and (2) atmospheric half-lives based on hydroxyl radical attack.

4.1.5 Fugacity Modeling

4.1.5.1 Modeling Methodologies

Fugacity-based multimedia fate modeling compares the relative distribution of chemicals among environmental compartments. A widely used model for this approach is the EQC model⁵.

There are multiple levels of the EQC model. In the document, "Determining the Adequacy of Existing Data", EPA states that it accepts Level I fugacity modeling to estimate transport/distribution values. The Agency states that Level III model data are considered "more realistic and useful for estimating a chemical's fate in the environment on a regional basis". The EQC Level I model utilizes input of basic chemical properties, including molecular weight, vapor pressure, and water solubility to calculate percent distribution within a standardized environment. EQC Level III uses these parameters to evaluate chemical distribution based on discharge rates into air, water, and soil, as well as degradation rates in air, water, soil, and sediment.

⁵ Equilibrium Criterion Model- Environmental Modeling Centre as developed by D. Mackay.

4.1.5.2 Summary of Available Data

There are no published or unpublished fugacity-based multimedia fate modeling data for members of the petroleum additive alkaryl sulfonate category. All of the members of this category have low vapor pressure and low water solubility indicating that they will not partition into the air or water to any great extent.

4.1.5.3 Test Plan for Fugacity

The HPV Challenge Program requires that fugacity modeling be performed or bridged to each member of a category. The relative distribution of substances within this category among environmental compartments will be evaluated using the Level I model. Data developed using a Level I model can then be used for simple comparative purposes across several substances. EQC Level III will not be used for this evaluation because appropriate emission levels are as yet unknown. Because of the physical nature of the substances in this category, a Level I dataset will be as equally robust as a Level III dataset and can then be used to assess the partitioning behavior of petroleum additive alkaryl sulfonates in the environment.

Input data to run the EQC Level I model will require an additional computer model to estimate physical/chemical properties from a structure. The model used for this purpose will be EPIWIN, version 3.02⁶, which was developed by the Syracuse Research Corporation. EPIWIN includes algorithms for estimating all physical and chemical properties needed for the EQC model.

Fifteen basic chemical structures will be used for this evaluation and will represent the twelve substances in this category. Representative structures will include C16 linear, C23 linear, C23 branched, di-C13 branched, C24 linear and C30 linear homologs. In addition, for selected substances, the high and low molecular weight range will be evaluated.

4.2 ECOTOXICOLOGY DATA

4.2.1 Aquatic Ecotoxicity Testing

4.2.1.1 Test Methodologies

Acute aquatic ecotoxicity tests are usually conducted with three species that represent three trophic levels in the aquatic environment: fish, invertebrates, and algae. The fish acute toxicity test (OECD Guideline 203, *Fish, Acute Toxicity Test*) establishes the lethality of a substance to a fish during a 96-hour exposure period. The acute invertebrate test (OECD Guideline 202, *Daphnia sp., Acute immobilization Test and Reproduction Test*) establishes the lethality of a substance to an invertebrate, typically a daphnid (*Daphnia magna*), during a 48-hour exposure period. The alga growth inhibition test (OECD Guideline 201, *Alga, Growth Inhibition Test*) establishes the potential of a

⁶ Environmental Science Center- Syracuse Research Corporation- EPI for windows.

substance to inhibit alga growth, typically using the freshwater unicellular green algae, *Pseudokirchneriella subcapitata* (formerly called *Selenastrum capricornutum*), during a 96-hour exposure period.

Three test methodologies are commonly used to conduct aquatic toxicity tests; i.e., flow-through, static, and static renewal tests.

Inflow-through tests, organisms are continually exposed to fresh chemical concentrations in each treatment level in the incoming water and there is greater assurance than with other test methods that the exposure levels and water quality remains constant throughout the test. Although flow-through testing is the preferred method, it is only applicable for chemicals that have adequate water solubility for testing.

In *static tests*, organisms are exposed in still water that is not renewed. The chemical is added to the dilution water to produce the desired test concentrations. Test organisms are then placed in the test chambers, and there is no change of water at any time during the test. There is less assurance that the test concentrations test organisms are exposed to will remain constant because test material can be adsorbed onto test chambers, degraded, volatilized, or otherwise changed during the test. Nevertheless, due to limitations of other test systems for non-volatile materials, the static test has been widely used, especially for testing organisms such as algae and *Daphnia*.

The *static-renewal test* is similar to a static test because it is conducted in still water, but the test solutions and control water are renewed periodically, usually every 24 hours. Daily test solution renewal provides a greater likelihood that the exposure concentrations will remain stable throughout the test. This is the preferred method for conducting aquatic toxicity tests for compounds such as the petroleum additive alkaryl sulfonates on fish. Daily renewals cannot be done in the algae test, and usually not in *Daphnia* tests, because the process of separation and replenishment would cause a discontinuity in the alga growth rate and it can stress, coat, or entrap *Daphnia* in any surface film during renewals. OECD considers the use of static test for fish, *Daphnia*, algae and the use of static renewal test for fish to be appropriate for testing poorly soluble chemicals like the petroleum additive alkaryl sulfonates provided that test solution preparation uses water accommodated fraction or water soluble fraction methods.⁷

4.2.1.2 Test Solution Preparation

Petroleum additive alkaryl sulfonates are poorly water-soluble substances, and it is not possible to prepare exposure solutions for aquatic toxicity testing by direct addition of

⁷ Organization for Economic Cooperation and Development (OECD) (2000). Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures. OECD Environmental Health and Safety Publications, Series on Testing and Assessment No.23, Paris, France.

measured quantities of test material to water. Two methods⁸ are used to prepare solutions of poorly water-soluble materials for aquatic toxicity testing:

- *Water accommodated fraction (WAF)* – This is a method in which the test solution contains only that fraction of the test material (organic phase) which is retained in the aqueous phase after a period of stirring long enough to reach equilibrium, followed by a sufficient time (1-4 hours) for phase separation. The WAF (aqueous phase) will contain soluble components of the test material at levels that will be dependent on the test material loading (the amount of material added to the aqueous medium). The resulting WAF is used in the aquatic toxicity test. Ideally, a WAF consists of a water-soluble extract of test material, but it can also include a stable micro-emulsion or contain small amounts of suspended matter.
- *Water soluble fraction (WSF)* This is a method in which a WAF is either filtered, centrifuged, or allowed to settle for a greater length of time (24 hours) than with the WAF method to remove suspended matter from the aqueous phase before being used in the aquatic toxicity test.

4.2.1.3 Reporting Toxicity Results

In both WAF and WSF tests, test material concentrations are expressed as loading rates (i.e., defined as the weight of test material added per unit volume of test medium during WAF or WSF preparation)⁹. For fish tests, endpoints can be expressed as median lethal loading rate (LL_{50}) when lethal effects occur to 50% of the test population or in cases where no lethal effects are observed at all loadings tested, LL_0 . In both cases, results can be expressed in mg/L and in studies where no lethality is observed, the result is expressed as LL_0 = the highest loading rate tested. For invertebrate and alga tests, endpoints are expressed as median effective loading rate (EL_{50}) or EL_0 in mg/L as discussed above.

Loading rates allow poorly water-soluble complex substances such as the petroleum additive alkaryl sulfonates to be compared to more readily soluble substances and /or pure chemicals on an equal basis. To allow comparison, the toxicity value is expressed as the amount of test material added per unit volume of water when preparing the WAF or WSF.

If test material exposure levels are analytically measured in the test, the endpoints can also be expressed as median lethal concentration (LC_{50}) or median effective concentration (EC_{50}) in mg/L. EC/LC_{50} s are often not reported because it is very difficult to accurately measure test material exposure levels that can be below 1.0 mg/L.

⁸ American Society for Testing and Materials (1998) D6081-98, Standard Practice for Aquatic Toxicity Testing of Lubricants: Sample Preparation and Results Interpretation.

⁹ Organization for Economic Cooperation and Development (OECD) (1999) Draft Guidance document on Aquatic Toxicity Testing of Difficult Substances. OECD, France.

NOTE: In this test plan, these results are reported as loading rates (EL/LL), to reflect the current reporting practices for the WAF method used in the tests. In the robust summaries, these data are presented as concentrations (EC/LC) as originally reported even though the test methods employed WAF preparation of test solutions without measurement of test material concentration.

4.2.2 Aquatic Toxicity of the Petroleum Additive Alkaryl Sulfonate Category

In general, the toxicity of a substance to an organism is limited by mechanisms of uptake and movement to target organs. Characteristics such as smaller molecular size and a lesser degree of ionization increase the ability of a substance to passively cross biological membranes. However, the soluble fraction of a compound in water represents the chemical fraction responsible for toxicity to aquatic organisms. Therefore, aquatic toxicity can be limited by the water solubility of a substance.

Data and preliminary modeling information indicates that all members of the petroleum additive alkaryl sulfonate category have low water solubility. The low water solubility suggests that the acute aquatic toxicity of these substances should be low due to limited bioavailability to aquatic organisms. However, the length of the alkyl side chains on these substances will influence their relative water solubility, and, hence, their relative toxicity. Modeling data indicate that the petroleum derived sodium salt (CAS # 68608-26-4) is predicted to be the most water-soluble member of the category and the member most likely to demonstrate potential aquatic toxicity.

4.2.2.1 Summary of Available Data

Acute aquatic ecotoxicity data for the petroleum additive alkaryl sulfonate category is summarized in Table 6. Four members of the category have been tested for acute aquatic toxicity in at least one species. A low order of toxicity was observed across the range of substances from those that contain the shortest alkyl side chain (C14) to the substances that contain the longest alkyl side chains.

4.2.2.1.1 Fish Acute Toxicity

Three of the twelve substances in the category and one structural analog were evaluated for acute toxicity to fish in five studies. Maximum test material loading rates were either 1,000 or 10,000 mg/L. No mortality was observed in any of the studies. Overall, the LL₅₀ for these substances was greater than 1000 mg/L indicating a relatively low order of toxicity to fish.

4.2.2.1.2 Invertebrate Acute Toxicity

Three of the twelve substances in the category were evaluated for acute toxicity to daphnids. The maximum test material loading rate was 1,000 mg/L. In general, minimal effects were observed in the studies. Overall, the EL₅₀ for these substances was greater than 1000 mg/L indicating a relatively low order of toxicity to daphnids.

4.2.2.1.3 Alga Toxicity

Three of the twelve substances in the category were evaluated for algal growth inhibition. Maximum test material loading rates were either 1,000 or 1,500 mg/L. The results indicate no observed toxicity to algae at or below 1,000 mg/L. In one test, there was an algistatic effect at 1,500 mg/L, which was reversed when the algae were placed in fresh media. Overall, the EL_{50} for these substances was greater than 1000 mg/L indicating a relatively low order of toxicity to algae.

4.2.2.2 Data Assessment and Test Plan for Acute Aquatic Ecotoxicity

In total, eleven adequate acute aquatic ecotoxicity studies have been conducted for the petroleum additive alkaryl sulfonate category. These studies involved three trophic levels of aquatic organisms and evaluated the acute aquatic ecotoxicity of five of the twelve members of the category. The substances tested ranged from ones with the shortest (C14) alkyl side chain to others with the longest alkyl side chains. The data consistently demonstrate a low order of acute aquatic ecotoxicity regardless of the length of the alkyl side chain. The similarity in the low order of toxicity for these substances is consistent with their similar chemical structure and physicochemical properties and supports the scientific justification of these twelve substances as a category within the HPV Challenge Program.

The HPV Challenge Program requires that an acute aquatic ecotoxicity test in fish, invertebrates, and algae be performed or bridged to each member of a category. Adequate data for all three species exist for two of the twelve substances. Additional testing and bridging will be used to fill the data gaps for the remaining ten substances.

- Petroleum derived sodium salt (CAS # 68608-26-4), which contains the shortest alkyl side chain (C14) in the category, will be evaluated for acute aquatic toxicity to fish, daphnids, and algae by conducting a limit test at 1000 mg/L. The results of these studies will be bridged to the other sodium salt in the category, which has similar physicochemical properties:
 - C 15-C30 alkaryl sodium salt derivative (CAS # 78330-12-8).
- The potential acute aquatic toxicity of petroleum derived calcium salt (CAS # 61789-86-4) to fish, daphnids, and algae will be determined by conducting a limit test at 1000 mg/L. The results of these tests will be bridged to the two remaining petroleum-derived substances in the category, which have similar physicochemical properties:
 - petroleum derived barium salt (CAS # 61790-48-5) and
 - petroleum derived calcium salt, overbased (CAS # 68783-96-O).

An additional limit test at 1000 mg/L will be performed on petroleum derived barium salt (CAS # 61790-48-5) as well.

- C 14-C24 alkaryl calcium salt derivative (CAS # 115733-09-o) will be evaluated for acute aquatic toxicity to fish by conducting a limit test at 1000 mg/L. The results of this test and the existing data for acute aquatic toxicity of this substance to daphnids and algae will be bridged to the other members of the category with similar chemical structures and physicochemical properties:

- C14-C24 alkaryl calcium salt, overbased derivative (CAS # 115733-10-3),
- C14-C24 alkaryl derivative (CAS # 115829-36-2), and
- C 16-C24 alkaryl calcium salt derivative (CAS # 70024-69-o).

The existing fish data for the C20-C24 alkaryl calcium salt, overbased derivative (CAS # 70024-7 1-4) analog of C1 6-C24 alkaryl calcium salt derivative (CAS # 70024-69-o) will be used to define the influence of longer alkyl chain lengths on aquatic toxicity for these substances.

- The existing data for mixed mono-C 15-C30 and di-C 11 -C 13 alkaryl calcium salt, overbased derivative (CAS # 71486-79-8) will be bridged to mixed mono-C15-C30 and di-C 1 I -C 13 alkaryl derivative (CAS # 7 1549-79-6).

4.3 MAMMALIAN TOXICOLOGY DATA

4.3.1 Physicochemical Properties Relevant to Mammalian Toxicity

Lipophilicity generally enhances the ability of chemicals to cross biological membranes. (either by passive diffusion or active transport via carrier proteins) to reach target tissues or receptors in an organism. Although alkaryl sulfonates are relatively large lipophilic compounds, and molecular size may be a critical limiting determinant for absorption, there is evidence in the published literature¹⁰ that these substances are absorbed. At the same time, the hydrophobic properties of petroleum additive alkaryl sulfonates suggest that, once they are absorbed, they would undergo limited distribution in the aqueous systemic circulation and reach potential target organs in limited concentrations. Biotransformation by mixed function oxidases often increases the water solubility of a substance, and data in the published literature¹¹ suggests that these substance undergo oxidation to metabolites with shorter alkyl side chains, which would enhance hydrophilicity. Finally, a chemical must have an active functional group that can interact chemically or physically with the target cell or receptor upon reaching it. For alkaryl sulfonates, the sulfonic acid moiety on an aromatic ring represents the only functional group that may have biological activity.

In addition to the general considerations discussed above, the low volatility of the members of this category indicate that, under normal conditions of use or transportation, exposure by the inhalation route is unlikely. In particular, the high viscosity of these substances suggests that it will be difficult to generate high concentration of respirable particles in the air.

Given the general lipophilic characteristic of these substances, the members of the category with the shortest alkyl side chains (C14) are the most likely to penetrate

¹⁰W.R. Michael, Metabolism of Linear Alkylate Sulfonate and Alkyl Benzene Sulfonate in Albino Rats. Toxicol. App. Pharmacol. 12,473-485 (1968).

¹¹ Reference E = W.R. Michael, Metabolism of Linear Alkylate Sulfonate and Alkyl Benzene Sulfonate in Albino Rats. Toxicol. App. Pharmacol. 12,473-485 (1968).

biological membranes. Despite the low water solubility of these substances, members of the category with the shortest alkyl side chain would also be the most hydrophilic and the most likely to be distributed in the systemic circulation and possibly reach a potential target organ.

4.3.2 Acute Mammalian Toxicity of the Petroleum Additive Alkaryl Sulfonate Category

4.3.2.1 Acute Toxicity Test Methodology

Acute toxicity studies investigate the effect(s) of a single exposure to a relatively high dose of a substance. Potential routes of exposure for acute toxicity assays include oral, dermal, and inhalation. Oral toxicity assays are conducted by administering test material to fasted animals (typically rats or mice) in a single gavage dose. Acute dermal toxicity tests are conducted by administering test material to the shaved skin on the back of the test animal (typically rats or rabbits) and allowing the test material to stay in contact with the skin application site for a specific duration (usually 24 hours). Acute inhalation toxicity assays are conducted by exposing test animals (typically rats) in a controlled atmosphere to a fixed air concentration of the test substance for a specific duration (typically 4 hours). The test material is either generated as a vapor or intentionally aerosolized into respirable particles, then metered into the exposure air at the desired concentration. Preferably, inhalation toxicity studies are conducted using either nose-only or head-only exposure to minimize potential confounding effects resulting from whole-body exposure. Whole body exposure may lead to over-prediction of inhalation toxicity hazard by increasing the body-burden of the test material through skin absorption or ingestion of test material as a consequence of grooming both during and after the inhalation exposure period.

Historically, lethality is a primary end-point of concern in acute toxicity studies, and the traditional index of oral and dermal potency is the median lethal dose that causes mortality in 50 percent of the test animals (LD_{50}). In acute inhalation studies, the traditional measurement of potency is the median lethal concentration of the test material in air that causes mortality in 50 percent of the test animals (LC_{50}). In addition to lethality, acute toxicity studies also provide insights regarding potential systemic toxicity through careful observation and recording of clinical signs and symptoms of toxicity as well as through detailed examination of tissues and organ systems.

Typically, acute oral and dermal toxicity studies are conducted using a limit dose of 5000 and 2000 mg/kg body weight, respectively, and acute inhalation toxicity studies are conducted using a limit dose of 5 mg/L for 4 hours (according to OECD and EPA testing guidelines). Prior to 1990, some acute dermal toxicity studies may have used a limit dose of 5000 mg/kg. Recently, harmonized EPA testing guidelines (August 1998) have set the limit dose for both oral and dermal acute toxicity studies at 2000 mg/kg body weight, while the recommended limit concentration for acute inhalation studies has been set at 2 mg/L for 4 hours. The limit dose test method minimizes the number of animals tested by exposing a single group of animals to a large dose (the limit dose) of the test substance. A

test substance that shows little or no effects at the limit dose is considered essentially nontoxic, and no further testing is needed. If compound-related mortality is observed at the limit dose, then further testing may be necessary.

4.3.2.2 Summary of Available Data

Acute toxicity data for the petroleum additive alkaryl sulfonate category is summarized in Table 7. Eight members of the category and one structural analog that have been tested for acute oral toxicity have a low order of toxicity. In addition, the three members of the category plus one structural analog tested for acute dermal toxicity and the one member of the category tested for acute inhalation toxicity also have a low order of toxicity. Thus, a low order of toxicity was observed across the range of substances from those that contain the shortest (C14) alkyl side chain to the substances that contain the longest alkyl side chains.

4.3.2.2.1 Acute Oral Toxicity

Eight of the twelve substances in the petroleum additive alkaryl sulfonate category and a C20-C24 alkaryl calcium salt derivative (no CAS #) analog of the C16-C24 alkaryl calcium salt (CAS # 70024-69-0) have been adequately tested for acute oral toxicity (OECD Guideline 401, *Acute Oral Toxicity*). In all but one of these studies, there were no deaths that could be attributed to treatment with the test material when administered at the limit dose of 2000 or 5000 mg/kg. In some studies, the primary clinical observations were diarrhea and reduced food consumption (without a change in body weight). These effects are consistent with the gastrointestinal actions of a detergent in an oil-based vehicle. In other studies, decreased body weight gain or ruffled fur was observed. In one study where deaths occurred, animals were administered dose levels well above the 2000 mg/kg limit dose. Overall, the acute oral LD₅₀ for these substances was greater than the 2000 mg/kg limit dose indicating a relatively low order of toxicity.

4.3.2.2.2 Acute Dermal Toxicity

Three of the twelve substances in the petroleum additive alkaryl sulfonate category and a C20-C24 alkaryl calcium salt derivative (no CAS #) analog of the C16-C24 alkaryl calcium salt (CAS # 70024-69-0) have been adequately tested for acute dermal (OECD Guideline 402, *Acute Dermal Toxicity*). No mortality was observed for any substance when administered at the limit dose of 2000 or 5000 mg/kg. The principal clinical observation was erythema and/or edema at the site of dermal application. In some cases, the cutaneous findings included dry, flaky skin, desquamation and hyperkeratosis. Overall, the acute dermal LD₅₀ for these substances was greater than the 2000 mg/kg limit dose indicating a relatively low order of toxicity.

4.3.2.2.3 Acute Inhalation Toxicity

One member of the petroleum additive alkaryl sulfonate category was tested for acute inhalation toxicity (OECD Guideline 403, *Acute Inhalation Toxicity*). Rats were exposed

whole-body to an aerosol of the substance at a nominal atmospheric concentration of 1.9 mg/L for four hours. This was the maximum attainable concentration due to the low volatility and high viscosity of the test material. No mortality was noted, and all animals fully recovered following depuration. Clinical signs of toxicity during exposure included reduced activity, matted coat, and closed eyes. Clinical signs of toxicity observed post exposure included lacrimation, nasal discharge, salivation, rales, matted coat, hunched appearance, soft stools and closed eyes. No treatment-related macroscopic findings were noted. The lack of mortality at a concentration just below the limit dose of 2.0 mg/L indicates a relatively low order of toxicity for this substance.

4.3.2.3 Data Assessment and Test Plan for Acute Mammalian Toxicity

In total, fourteen adequate acute toxicity studies have been conducted for the petroleum additive alkaryl sulfonate category. These studies involved two species of laboratory animals (rats or rabbits); three routes of exposure (oral, dermal, and inhalation); and evaluated the toxicity of eight of the twelve members of the category and one structural analog. The substances tested ranged from ones with the shortest (C14) alkyl side chain to others with the longest alkyl side chains. The data consistently demonstrate a low order of acute toxicity regardless of the length of the alkyl side chain. The similarity in the low order of toxicity for these substances is consistent with their similar chemical structure and physicochemical properties and supports the scientific justification of these twelve substances as a category within the HPV Challenge Program.

The HPV Challenge Program requires that either an acute oral (preferable), dermal, or inhalation test be performed or bridged to each member of a category. Adequate acute oral toxicity tests exist for eight of the twelve substances in the petroleum additive alkaryl sulfonate category. Bridging will be used to fill the data gaps for the remaining four substances.

- Acute oral toxicity data for C14-C24 alkaryl calcium salt derivative (CAS # 115733-09-0) will be bridged to the other members of the category with similar chemical structures and physicochemical properties:
 - C14-C24 alkaryl acid derivative (CAS # 115829-36-2),
 - C 14-C24 alkaryl calcium salt, overbased derivative (CAS # 115733-10-3),
 - Cl 6-C24 alkaryl calcium salt derivative (CAS # 70024-69-0),
- Acute oral toxicity data for C 14- C24 alkaryl calcium salt derivative (CAS # 115733-09-0), which contains the shortest alkyl side chains in the category, will also be bridged to the remaining substance in the category, which has the longest alkyl side chains, due to the lack of an upward trend in toxicity over the range of alkyl side chain lengths that have been tested:
 - mixed mono-C15-C30 and di-C11-C13 alkaryl calcium salt, overbased derivative (CAS # 71486-79-8).

By bridging these data to the four untested substances, the acute toxicity of the category has been evaluated adequately with respect to all acute toxicity endpoints, and no additional acute toxicity testing is proposed for the HPV Challenge Program

4.3.3 Mutagenicity of the Petroleum Additive Alkaryl Sulfonate Category

4.3.3.1 Mutagenicity Test Methodology

Genetic toxicology is concerned with the effects of substances on genetic material (i.e., DNA and chromosomes). Within genetic material, the gene is the simplest **functional** unit composed of DNA. Mutations are generally nonlethal, heritable changes to genes which may arise spontaneously or as a consequence of xenobiotic exposure. Genetic mutations are commonly measured in bacterial and mammalian cells. The simplest test systems measure the occurrence of a base-pair substitution mutation in which a single nucleotide is changed followed by a subsequent change in the complementary nucleotide on the other DNA strand. Frame shift mutations occur following the deletion or insertion of one or more nucleotides, which then changes the “reading frame” for the remainder of the gene or multiple genes. Genetic testing for these types of point mutations is generally accomplished by *in vitro* cellular assays for forward or reverse mutations. A forward mutation occurs when there is a detectable change in native DNA whereas a reverse mutation occurs when a mutated cell is returned to its initial phenotype. Both base-pair substitutions and frame shift mutations are routinely measured in bacterial cells by measuring the ability of a cell to acquire the capability to grow in an environment missing an essential amino acid. In these tests, a large number of cells are examined to demonstrate a significant increase in the frequencies of mutations that occur over the frequency of spontaneous mutations.

Chromosomal aberrations are large scale numerical or structural alterations in eukaryotic chromosomes including deletions (visualized as breaks), translocations (exchanges), non-disjunction (aneuploidy), and mitotic recombination. Chromosomal breakage is the classical end point in chromosomal aberration assays. Substances that induce structural changes in chromosomes, especially chromosome breaks, are referred to as “clastogens.” To visualize chromosomes and chromosomal aberrations following *in vitro* or *in vivo* treatment with a substance, cells are arrested in metaphase, treated to swell the chromosomes, fixed, transferred to slides and stained. The first metaphase following treatment is the time at which the greatest number of cells with damaged chromosomes may be observed. The most frequently used test systems investigate changes in mammalian cells (such as Chinese hamster ovary or lung cells; human or rat lymphocytes; or human, rat or mouse bone marrow cells) following either *in vitro* or *in vivo* exposure to the test substance. The micronucleus test is a common *in vivo* assay that measures the frequency of micronuclei formation (i.e., chromosomal fragments) in polychromatic erythrocytes.

4.3.3.2 Summary of Mutagenicity Data

A summary of the mutagenicity information for the petroleum additive alkaryl sulfonate category is presented in Table 8. Either bacterial or mammalian gene mutation assays, *in vitro* chromosomal aberration assays, or *in vivo* chromosomal aberration assays have been conducted for two of the twelve members of the category and two structural analogs. Neither mutagenicity nor clastogenicity was exhibited by any of the substances

in the referenced tests with or without metabolic activation. Neither mutagenicity nor clastogenicity was observed across the range of materials from those that contain the shortest (C14) alkyl side chain to the substances that contain the longer alkyl side chains.

4.3.3.2.1 Bacterial Gene Mutation Assay

Two of the twelve substances in this category and two structural analogs, a C20-C24 alkaryl calcium salt derivative (no CAS #) analog of the C16-C24 alkaryl calcium salt (CAS # 70024-69-0) and a C15-C21 alkaryl sodium salt derivative (no CAS #) analog of C15-C30 alkaryl sodium salt derivative (CAS # 78330-12-8), have been adequately tested in a *Bacterial Reverse Mutation Test* (OECD Guidelines 471 and/or 472). All tested substances were negative for mutagenic activity, with and without metabolic activation.

4.3.3.2.2 Mammalian Gene Mutation Assay

One substance in this category has been adequately tested in a mouse lymphoma cell assay (OECD Guideline 476, *In Vitro Mammalian Cell Gene Mutation Test*). The results of this study were negative for mutagenic activity with and without metabolic activation of the test substance.

4.3.2.2.3 In vivo Chromosomal Aberration Assays

Two of the twelve substances in this category and a C20-C24 alkaryl calcium salt derivative (no CAS #) analog of the C16-C24 alkaryl calcium salt (CAS # 70024-69-0) have been adequately tested in an *in vivo* chromosomal aberration assay. These studies were conducted using bone marrow cells from mice that were dosed by oral gavage or intraperitoneal injection (OECD Guideline 474, *Mammalian Erythrocyte Micronucleus Test*). All test substances were negative for clastogenicity.

4.3.2.2.4 In vitro Chromosomal Aberration Assay

Two substances have been adequately tested in an *in vitro* chromosomal aberration assay using Chinese hamster ovary cells (OECD Guideline 473, *In Vitro Mammalian Chromosome Aberration Test*). The results of these studies, performed with and without metabolic activation of the test material, were negative for clastogenicity.

4.3.3.3 Data Assessment and Test Plan for Mutagenicity

Two of the twelve members of the petroleum additive alkaryl sulfonate category and two structural analogs have been tested for mutagenicity in ten tests for gene mutations and chromosomal aberrations. The assays included point mutations in bacterial or mammalian cells, *in vitro* chromosomal aberrations in mammalian cells, and *in vivo* chromosomal aberrations in mice. The substances tested ranged from one with the shortest (C14) alkyl side chain to others with the longest alkyl side chains. The data consistently demonstrate no evidence of genotoxicity regardless of the length of the alkyl side chain. This suggests

that all members of the category lack genotoxicity due to their similarity in chemical structures and physicochemical properties and supports the scientific justification of these twelve substances as a category within the HPV Challenge Program.

The HPV Challenge Program requires that a gene mutation and a chromosomal aberration test be performed or bridged to each member of a category. Adequate gene mutation and chromosomal aberration tests exist for two of the twelve substances in the petroleum additive alkaryl sulfonate category and one structural analog. Bridging will be used to fill the data gaps for the remaining ten substances.

- Data for petroleum derived calcium salt overbased (CAS # 68783-96-O) will be bridged to the other three petroleum-derived substances in the category:
 - petroleum derived calcium salt (CAS # 61789-86-4),
 - petroleum derived sodium salt (CAS # 68608-26-4), and
 - petroleum derived barium salt (CAS # 6 1790-48-5).
- Data for petroleum derived calcium salt overbased (CAS # 68783-96-O) will also be bridged to the other seven members of the category, which have similar chemical structures and physicochemical properties:
 - C14-C24 alkaryl calcium salt derivative (CAS # 115733-09-O),
 - C14-C24 alkaryl calcium salt, overbased derivative (CAS # 115733-10-3),
 - C14-C24 alkaryl acid derivative (CAS # 115829-36-2),
 - C15-C30 alkaryl sodium salt derivative (CAS # 78330-12-8),
 - mixed mono-C I 5-C30 and di-C I I -C13 alkaryl derivative (CAS # 71549-79-6),
 - mixed mono-C I 5-C30 and di-C 11 -C 13 alkaryl calcium salt, overbased derivative (CAS # 71486-79-8), and
 - C16-C24 alkaryl calcium salt derivative (CAS # 70024-69-o).

This is justified since there is no upward trend in genotoxicity between the petroleum derived calcium salt overbased, which contains the shortest alkyl side chain (C14), and the C20-C24 alkaryl calcium salt derivative (no CAS #) analog of C16-C24 alkaryl calcium salt (CAS # 70024-69-0), which defines the genotoxicity of the members of the category with the longer alkyl side chain lengths.

By bridging these data to the ten untested substances, the category has been evaluated adequately for genotoxicity, and no additional testing is proposed for the HPV Challenge Program.

4.3.4 Repeated-dose Toxicity of the Petroleum Additive Alkaryl Sulfonate Category

4.3.4.1 Repeated-dose 'Toxicity Test Methodology

Repeated-dose toxicity studies evaluate the systemic effects of repeated exposure to a chemical over a significant period of the life span of an animal (rats, rabbits, or mice). Chronic repeated-dose toxicity studies are concerned with potential adverse effects upon exposure over the greater part of an organism's life span (e.g., one to two years in rodents). Subchronic repeated-dose studies are also concerned with effects caused by exposure for an extended period, but not one that constitutes a significant portion of the

expected life span. Subchronic studies are useful in identifying target organ(s), and they can be used in selecting dose levels for longer-term studies. Typically, the exposure regimen in a subchronic study involves daily exposure (at least 5 consecutive days per week) for a period of at least 28 days or up to 90 days (i.e., 4 to 13 weeks). A recovery period of two to four weeks (generally included in most study designs) following completion of the dosing or exposure period provides information on whether or not the effects seen during the exposure period are reversible upon cessation of treatment. The dose levels evaluated in repeated-dose toxicity studies are notably lower than the relatively high limit doses used in acute toxicity studies. The NOAEL (no observed adverse effect level), usually expressed in mg/kg/day, defines the dose of test material that produced no significant toxicological effects. If the test material produce toxicity at the lowest dose tested (i.e., there is no defined NOAEL), the lowest dose that produced an adverse effect is defined as the LOAEL (lowest observed adverse effect level). While these studies are designed to assess systemic toxicity, the study protocol can be modified to incorporate evaluation of potential adverse reproductive and/or developmental effects.

Reproductive and developmental toxicity studies generate information on the effects of a test substance on male and female reproductive performance such as gonadal function, mating behavior, conception, and development of the conceptus, parturition, and post-partum development of the offspring. Various study designs exist, but they all involve exposure to both male and female test animals before mating. The rat is most often selected as the test species. The test substance is administered to males and females continuously at several graduated doses for at least two weeks prior to mating and until the animals are sacrificed. The males are treated for at least two more weeks. Male gonadal histopathology is carefully assessed at the end of the study. The females are treated through parturition and early lactation. The adult females and offspring are typically studied until termination on post-natal day 21, or sometimes earlier. In addition to providing data on fertility and reproduction, this study design provides information on potential developmental toxicity following prenatal and limited post-natal exposure to the test substance. An NOAEL or LOAEL is also used to describe the results of these tests, with the exception that these values are derived from effects specific to reproduction or development.

The “toxicity to reproduction” requirement in the HPV Challenge Program can be met by conducting the *Reproduction/Developmental Toxicity Screening Test* (OECD Guideline 421) or by adding this screening test to a repeated-dose study (OECD Guideline 422, *Combined Repeated Dose Toxicity Study with the Reproductive/Developmental Toxicity Screening Test*). The *One-Generation Reproduction Toxicity Study* (OECD Guideline 415) is a more comprehensive protocol for the study of the effect of a test material on reproduction and development that also meets the OECD SIDS and the HPV Challenge Program requirements.

4.3.4.2 Summary of Repeated-Dose Toxicity Data

A summary of the results from the repeated-dose studies for the petroleum additive alkaryl sulfonate category is presented in Table 9. Repeated-dose toxicity tests have been

performed on three members of the petroleum additive alkaryl sulfonate category by three routes of administration and in two species of laboratory animals, rats and rabbits. Repeated oral administration to rats caused decreased serum cholesterol levels at the highest dose tested, 1000 mg/kg/day. Repeated inhalation exposure to rats caused adverse effects on the lungs. Repeated dermal administration to rats and rabbits caused inflammatory skin changes following repeated skin contact, but there were no systemic effects in rats. Systemic effects observed in rabbits following repeated dermal administration include reduction in hematological parameters and evidence of liver injury. The adverse effects on male reproductive organs were observed only in rabbits after repeated dermal application of dose levels that were irritating to the skin.

4.3.4.2.1 Systemic Toxicity Tests

Two of the 12 substances in the alkaryl sulfonate category and a structural analog have been tested for subchronic toxicity in five studies.

Petroleum derived calcium salt, over-based (CAS # 68783-96-O) was evaluated in a 28-day repeated-dose dermal toxicity study in rats (OECD Guideline 410, *Repeated Dose Dermal Toxicity: 21/28 Day*). The substance was applied topically at doses of 100, 300, and 1000 mg/kg/day under occlusive dressing six hours/day for 28 consecutive days. A low incidence of erythema, desquamation and scabbing was sporadically observed in treated animals. The NOAEL for systemic toxicity for this study was 1000 mg/kg/day.

Petroleum derived calcium salt, overbased (CAS # 68783-96-O) was also evaluated in a 28-day inhalation toxicity study in rats (OECD Guideline 412, *Repeated Dose Inhalation Toxicity: 28/14 Day*). Inhalation exposures were six hours/day, five days/week for four weeks at actual whole-body exposure concentrations of 49.5, 156 and 260 mg/m³. The experimental animals were observed to have red nasal discharge, matted coat and decreased activity at the two highest dose levels. Dose-related increases in lung weight were accompanied by microscopic evidence of intralobular macrophage accumulation and bronchiole epithelial hyperplasia/hypertrophy. Based on the latter findings, the NOAEL was 49.5 mg/m³.

A C20-C24 alkaryl calcium salt derivative (no CAS #) analog of C16-C24 alkaryl calcium salt derivative (CAS # 70024-W-O) was evaluated in a 28-day repeated-dose oral toxicity study in rats (OECD Guideline 407, *Repeated Dose 28-Day Oral Toxicity Study in Rodents*). The substance was administered at 100, 500 and 1000 mg/kg/day for 28 consecutive days. Serum chemistry analysis revealed significant reductions in cholesterol in the high dose male and female groups. Based on the reduction in mean serum cholesterol, the NOAEL was 500 mg/kg/day.

Alkaryl magnesium salt derivative (CAS # 7 1786-47-5) was evaluated in a 28-day repeated-dose dermal toxicity study in rats (OECD Guideline 410). The substance was applied topically at doses of 100, 300 or 1000 mg/kg under occlusive dressing six hours/day for 28 consecutive days. Local cutaneous responses, characterized by

desquamation and hyperkeratosis were seen in some rats. The NOAEL for systemic toxicity for this study was 1000 mg/kg/day.

Alkaryl magnesium salt derivative (CAS # 7 1786-47-5) was also evaluated in a 28-day repeated-dose dermal toxicity study in rabbits (OECD Guideline 410). The substance was applied topically at a dose volume of 2 ml/kg/day and concentrations of 0, 25, or 100% (w/v) in Primol 205 for six hours/day, five days/week for 20 days. Local irritation responses (i.e., edema, erythema, desquamation, fissuring, and hyperkeratosis) were observed at the site of treatment in both dose groups. Systemic findings included significant reductions in hematological parameters (hemoglobin, hematocrit, erythrocyte count and leukocyte count) in the high dose group. Reduction in total plasma protein (including globulin) and increases in serum alkaline phosphatase, SGPT, and SGOT levels were observed in both treatment groups. Elevations in the serum levels of hepatic enzymes were accompanied by increases in liver weights in both treatment groups, but histopathological lesions (multifocal hepatocellular degeneration) were observed only in the high dose group. Testes and epididymides weights were also reduced in both treatment groups. Microscopic changes observed in the high dose group included aspermatogenesis and multifocal tubular hypoplasia in the testes and epithelial hypoplasia in the epididymides. Due to the observation of adverse effects at both dose levels, an NOAEL was not established in this study.

4.3.4.2.2 Reproductive/Developmental Toxicity

No reproductive or developmental toxicity data considered adequate under the HPV Challenge Program are available for the petroleum additive alkaryl sulfonate category.

4.3.4.2 Data Assessment and Test Plan for Repeated-dose Toxicity

Five repeated-dose toxicity studies using two different animal species, rats and rabbits, have been conducted with two of the twelve category members and one structural analog of a substance in this category. The substances tested ranged from one with the shortest (C14) alkyl side chain to others with the longer alkyl side chains. In rats, repeated oral administration caused minimal systemic toxicity. Repeated dermal application caused local skin injury at the site of application, and repeated inhalation caused local injury to the lungs. In rabbits, repeated dermal application caused severe skin irritation, liver toxicity, and reproductive organ toxicity that was not observed in rats. The liver toxicity, which occurred only at the high dose level in rabbits, may have been due to the differences in dose selection between the rat and rabbit studies. The high dose in the rat studies was the limit dose of 1000 mg/kg/day, but the high dose in the rabbit study, approximately 2.28 g/kg/day, exceeded the limit dose. The adverse effects on male reproductive organs appear to be a specific response of the rabbit to the effects of severe cutaneous irritation rather than a systemic response to a toxic xenobiotic. Changes in male reproductive organs in the rabbit have been observed when other irritating

substances are applied to the skin at dose levels that cause skin lesions.^{12,13} These effects appear to be specific to the rabbit, since similar effects were not observed in rats following repeated dermal application of dose levels that were irritating to the skin. Therefore, the data from the rat studies demonstrate no evidence of repeated-dose toxicity, regardless of the length of the alkyl side chain, at dose levels at or below the limit dose of 1000 mg/kg/day.

The HPV Challenge Program requires that a repeated-dose toxicity study and a reproductive toxicity study be performed or bridged to each member of a category. Adequate data for repeated-dose toxicity exist for two of the twelve substances in the petroleum additive alkaryl sulfonate category. Bridging can be used to fill the data gaps for the remaining ten substances.

- The repeated-dose toxicity data for petroleum derived calcium salt, overbased (CAS # 68783-96-O) can be bridged to the other three petroleum-derived substances in the category:
 - petroleum derived calcium salt (CAS # 61789-86-4),
 - petroleum derived sodium salt (CAS # 68608-26-4), and
 - petroleum derived barium salt (CAS # 61790-48-5).
- The repeated-dose toxicity data for petroleum derived calcium salt, overbased (CAS # 68783-96-O) can also be bridged to the other seven members of the category, which have similar chemical structures and physicochemical properties:
 - C 14-C24 alkaryl calcium salt derivative (CAS # 115733-09-O),
 - C 14- C24 alkaryl calcium salt, overbased derivative (CAS # 115733- 1 0-3),
 - C 14-C24 alkaryl acid derivative (CAS # 115829-36-2),
 - C15-C30 alkaryl sodium salt derivative (CAS # 78330-12-8),
 - mixed mono-C15-C30 and di-Cl 1-Cl3 alkaryl derivative (CAS # 71549-79-6),
 - mixed mono-C15-C30 and di-Cl1-Cl3 alkaryl derivative (CAS # 71486-79-8), and
 - C16-C24 alkaryl calcium salt derivative (CAS # 70024-69-o).

This is justified since there is no upward trend in repeated-dose toxicity between the petroleum derived calcium salt overbased, which contains the shortest alkyl side chain (C14), and the C20-C24 alkaryl calcium salt derivative (no CAS #) analog of C16-C24 alkaryl calcium salt (CAS # 70024-69-O), which defines the toxicity of the members of the category with the longer alkyl side chain lengths.

However, since a reproductive toxicity study will need to be conducted for the alkaryl sulfonate category (as discussed below), a 28-day repeated-dose oral toxicity will be

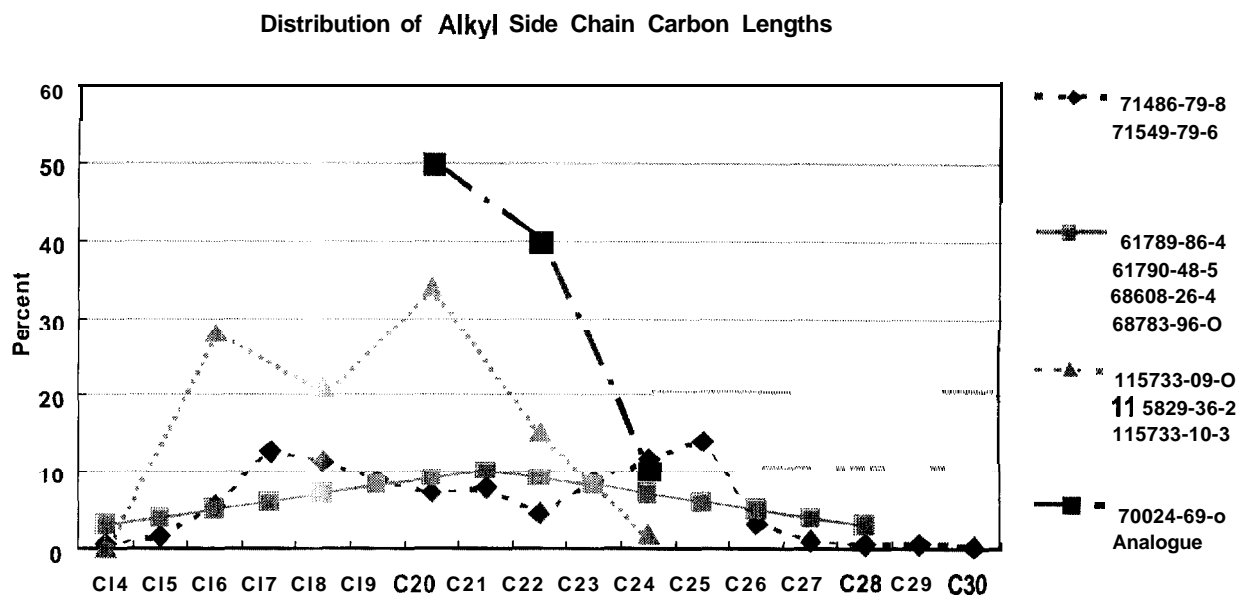
¹²Wong, Z. A., VonBurg, R., Spangler, W. L., and MacGregor, J. A. (1982) Testicular Damage in the Rabbit Resulting from Simple Chemical Cutaneous Irritation. *The Toxicologist* 2: 4 1.

¹³McKee, R. H., Kapp, Jr., R. W., and Ward, D. P. (1985) Evaluation of the Systemic Toxicity of Coal Liquefaction-Derived Materials Following Repeated Dermal Exposure in the Rabbit. *J. App. Toxicol.* 5: 345-351.

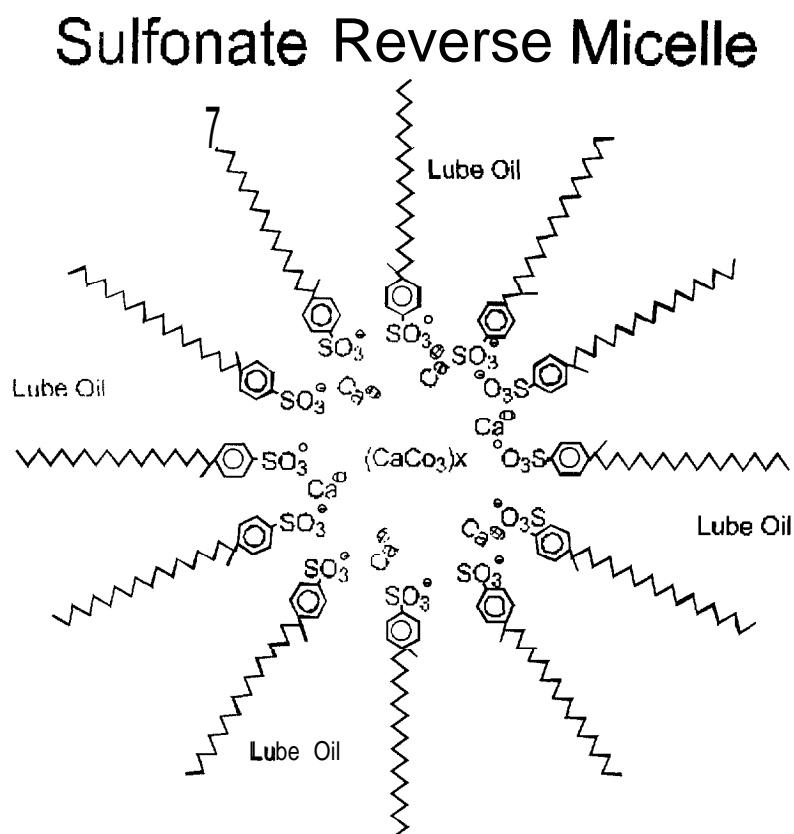
conducted with the C14-24 alkaryl calcium salt (CAS # 115733-09-o) in order to select appropriate dose levels for the reproductive toxicity study. The data from this study will also better define the repeated-dose toxicity of the category members with the shortest alkyl side chains by the oral route of exposure,

Although the petroleum additive alkaryl sulfonate category is well tested for other health effects, no reproductive or developmental toxicity studies considered to be adequate under the HPV Challenge Program are available for the members of the petroleum additives alkaryl sulfonate category. Thus, the reproductive toxicity potential of the petroleum additive alkaryl sulfonates will be evaluated with a one-generation test (OECD Guideline 415) using C 14-C24 alkaryl calcium salt derivative (CAS # 115733-09-o) and the results will be bridged to the other members of the category. This material has been selected because it contains the highest proportion of fractions with the shortest alkyl chain length in the category.

FIGURE 1. PERCENTAGE OF EACH CARBON CHAIN NUMBER IN ALKYL
SIDE CHAIN



**FIGURE 2. GENERAL STRUCTURE OF A PETROLEUM ADDITIVE
ALKARYL SULFONATE REVERSE MICELLE**



GA10228 • Sulfonate Reverse Micelle • ch • 1/24/01

TABLE 1. MEMBERS OF THE PETROLEUM ADDITIVE ALKARYL SULFIDE CATEGORY

CAS Number	Chemical Name	Simplified Chemical Name
61789-86-4	Sulfonic acids, petroleum, calcium salts	Petroleum derived calcium salt
61790-48-5	Sulfonic acids, petroleum, barium salts	Petroleum derived barium salt
68608-26-4	Sulfonic acids, petroleum, sodium salts	Petroleum derived sodium salt
68783-96-0	Sulfonic acids, petroleum, calcium salts, overbased	Petroleum derived calcium salt, overbased
70024-69-0	Benzenesulfonic acid, mono-C 16-C24 alkyl derivatives, calcium salts	C16-C24 alkaryl calcium salt derivative
71486-79-8	Benzenesulfonic acid, mono-C15-C30 branched alkyl and di-C11-C13 branched and linear alkyl derivatives, calcium salts, overbased	Mixed mono-C 15-C30 and di-C 11-C 13 alkaryl calcium salt, overbased derivative
71549-79-6	Benzenesulfonic acid, mono-C15-C30 branched alkyl and di-C 11 -C 13 branched and linear alkyl derivatives	Mixed mono-C 15-C30 and di-C 11 -C 13 alkaryl derivative
71786-47-5	Benzenesulfonic acid, mono and dialkyl derivatives, magnesium salts	Alkaryl magnesium salt derivative
78330-12-8	Benzenesulfonic acid, C15-C30 alkyl derivatives, sodium salts	C15-C30 alkaryl sodium salt derivative
115733-09-0	Benzenesulfonic acid, C14-C24 branched and linear alkyl derivatives, calcium salts	C14-C24 alkaryl calcium salt derivative
115733-10-3	Benzenesulfonic acid, C 14-C24 branched and linear alkyl derivatives, calcium salts, overbased	C14-C24 alkaryl calcium salt, overbased derivative
115829-36-2	Benzenesulfonic acid, C14-C24 branched and linear alkyl derivatives	C14-C24 alkaryl derivative

**TABLE 2. CHEMICAL STRUCTURES OF PETROLEUM ADDITIVE
ALKARYL SULFONATES**

CAS Number	Chemical Structure
61789-86-4	$\left(\begin{array}{c} \text{alkyl aromatic} \\ \text{MW= 300-400} \end{array} \text{---SO}_3 \right)_2 \text{---Ca}$
6 1790-48-5	$\left(\begin{array}{c} \text{alkyl aromatic} \\ \text{MW= 350-450} \end{array} \text{---SO}_3 \right)_2 \text{---Ba}$
68608-26-4	$\begin{array}{c} \text{alkyl aromatic} \\ \text{MW= 300-400} \end{array} \text{---SO}_3 \text{---Na}$
68783-96-O	$\left[\left(\begin{array}{c} \text{alkyl aromatic} \\ \text{MW= 350-450} \end{array} \text{---SO}_3 \right)_2 \text{---Ca} \right]_y \cdot \left(\text{CaCO}_3 \right)_x$
7002469-O	$\left(\begin{array}{c} \text{SO}_3 \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{C}_{16-24} \text{ linear} \end{array} \right)_2 \text{---Ca}$
71486-79-8	$\left[\left(\begin{array}{c} \text{SO}_3 \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{C}_{15-30} \text{ branched} \end{array} \right)_2 \text{---Ca} \right]_y \cdot \left(\text{CaCO}_3 \right)_x + \left[\left(\begin{array}{c} \text{SO}_3 \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{C}_{1-13} \text{ branched and linear} \end{array} \right)_2 \text{---Ca} \right]_y \cdot \left(\text{CaCO}_3 \right)_x$

TABLE 2. CHEMICAL STRUCTURE S OF PETROLEUM ADDITIVE ALKYL SULFONATE (CONT.)

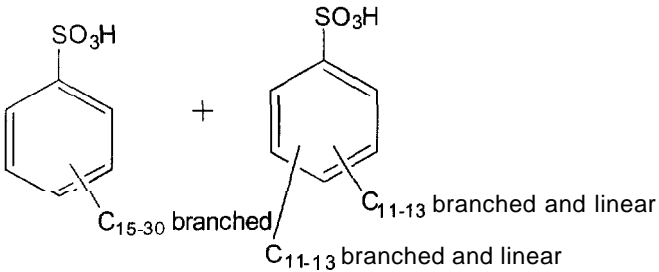
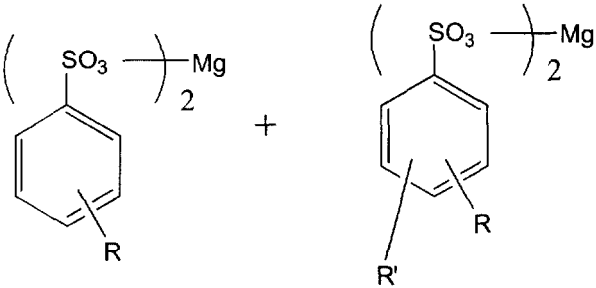
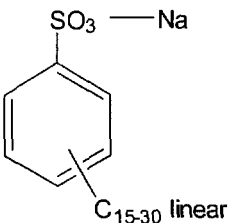
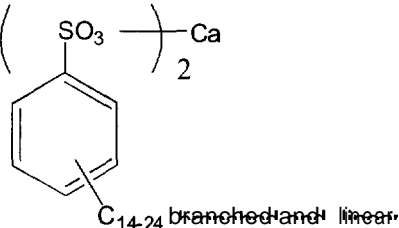
CAS Number	Chemical Structure
71549-79-6	 <p> C_{15-30} branched C_{11-13} branched and linear C_{11-13} branched and linear </p>
71786-47-5	 <p>+ the mixed mono and dialkylbenzenesulfonic acid salts</p>
78330-12-8	 <p>C_{15-30} linear</p>
115733-09-0	 <p>C_{14-24} branched and linear</p>

TABLE 2. CHEMICAL STRUCTURE S OF PETROLEUM ADDITIVE ALKYL SULFONATE (CONT.)

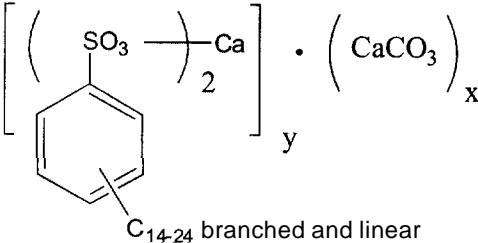
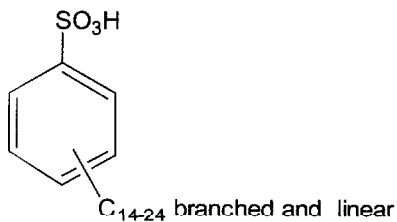
CAS Number	Chemical Structure
115733-10-3	 <p>$\left[\left(\text{SO}_3 - \text{C}_{14-24} \right)_2 \text{Ca} \right]_y \cdot \left(\text{CaCO}_3 \right)_x$</p> <p>C₁₄₋₂₄ branched and linear</p>
115829-36-2	 <p>SO_3H</p> <p>C₁₄₋₂₄ branched and linear</p>

TABLE 3. PHYSICOCHEMICAL PROPERTIES OF PETROLEUM ADDITIVE ALKARYL SULFONATES

CAS Number	Equivalent Weight ¹	Carbon Number Range	Specific Gravity ² g/ml	Viscosity ³ cSt @ 100 °C	Melting Point ⁴ °C	Boiling Point ⁵ °C	Vapor Pressure ⁶ Pa	Water Solubility mg/L	Log Kow
115829-36-2	354-494	C14-C24	No data	No data	208.45	506.34	<1X10 ⁻¹⁰	No data ⁷	No data ⁷
115733-09-0	393-533	C14-C24	No data	No data	349.84	935.88	<1X10 ⁻¹⁰	No data ⁷	No data ⁷
115733-10-3	393-533	C14-C24	No data	No data	349.84	935.88	<1X10 ⁻¹⁰	No data ⁷	No data ⁷
68608-26-4	376-600	C14-C30	No data	No data	309.31	707.03	<1X10 ⁻¹⁰	No data ⁸	No data ⁷
61789-86-4	393-617	C14-C30	0.977	175	349.84	935.88	<1X10 ⁻¹⁰	No data ⁷	No data ⁷
68783-96-0	393-617	C14-C30	1.165	190	349.84	935.88	<1X10 ⁻¹⁰	No data ⁷	No data ⁷
61790-48-5	490-714	C14-C30	No data	No data	349.84	935.88	<1X10 ⁻¹⁰	No data ⁷	No data ⁷
78330-12-8	390-600	C15-C30	No data	No data	347.25	788.26	<1X10 ⁻¹⁰	No data ⁸	No data ⁷
71549-79-6	368-578	C15-C30	No data	No data	208.45	506.34	<1X10 ⁻¹⁰	0.075	>6.7
71486-79-8	407-617	C15-C30	No data	No data	341.76	776.50	<1X10 ⁻¹⁰	No data ⁷	No data ⁷
70024-69-0	421-533	C16-C24	No data	No data	349.84	935.88	<1X10 ⁻¹⁰	<0.100	>6.0
71786-47-5	461-517	C20-C24	1.142	225	349.84	935.88	<1X10 ⁻¹⁰	No data ⁷	No data ⁷

¹Equivalent weight = molecular weight of one alkylbenzene sulfonic acid plus molecular weight of metal.

²ASTM D1298-99, Standard Test Method for Density, Relative Density (Specific Gravity), or API Gravity of Crude Petroleum and Liquid Petroleum Products by Hydrometer Method

³ASTM D 445-97, Standard Test Method for Kinematic Viscosity of Transparent and Opaque Liquids (the Calculation of Dynamic Viscosity)

⁴Modeling data; melting point cannot be measured due to viscosity of liquid.

⁵Modeling data; boiling point cannot be determined because substance decomposes before it boils.

⁶"De-oiled" petroleum additive alkaryl sulfonates are solid. As manufactured, vapor pressure is estimated from the vapor pressure of the petroleum base stock in which the substance is manufactured.

⁷No data needed; bridging from other members of the category.

*Testing for water solubility will be conducted.

TABLE 4. EVALUATION OF ENVIRONMENTAL FATE INFORMATION FOR PETROLEUM ADDITIVE ALKARYL SULFONATES

CAS Number	BIODEGRADABILITY	HYDROLYSIS	PHOTODEGRADATION
	Available Data & Proposed Testing	Available Data & Proposed Testing	Available Data & Proposed Testing
115829-36-2	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
115733-09-0	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
115733-10-3	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
68608-26-4	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
61789-86-4	8.6% biodegraded after 28 days	No testing needed'	AOPWIN Model Estimation
68783-96-0	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
61790-48-5	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
78330-12-8	Test	No testing needed'	AOPWIN Model Estimation
7 1549-79-6	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
7 1486-79-8	8.6% biodegraded after 28 days	No testing needed'	AOPWIN Model Estimation
70024-69-o	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation
C20-C24 alkaryl calcium salt derivative (no CAS #) analog of 70024-69-O	8.0% biodegraded after 28 days	No testing needed'	No estimation needed for analogs
71786-47-5	No testing needed Bridging	No testing needed'	AOPWIN Model Estimation

'See technical discussion of information presented in Table 5.

**TABLE 5. FUNCTIONAL GROUP, CHEMICAL CLASSES, AND HYDROLYTIC POTENTIAL OF PETROLEUM
ADDITIVE ALKARYL SULFONATES**

CAS Number	Functional Group and Chemical Class	Potential for Hydrolysis
115829-36-2	Aromatic benzene ring	Low
115733-09-0	Branched hydrocarbon chain	LOW
115733-10-3	Linear hydrocarbon chain	Low
	Sulfonic acid	Low
68608-26-4	Aromatic benzene ring	Low
61789-86-4	Branched hydrocarbon chain	LOW
68783-96-0	Linear hydrocarbon chain	Low
61790-48-5	Sulfonic acid	Low
78330-12-x	Aromatic benzene ring	LOW
	Linear hydrocarbon chain	LOW
	Sulfonic acid	Low
71549-79-6	Aromatic benzene ring	LOW
71486-79-8	Branched hydrocarbon chain	Low
	Linear hydrocarbon chain	LOW
	Sulfonic acid	LOW
70024-69-0	Aromatic benzene ring	LOW
	Linear hydrocarbon chain	LOW
	Sulfonic acid	LOW
71786-47-5	Aromatic benzene ring	Low
	Branched hydrocarbon chain	LOW
	Linear hydrocarbon chain	Low
	Sulfonic acid	Low

TABLE 6. EVALUATION OF AQUATIC TOXICOLOGY OF PETROLEUM ADDITIVE ALKARYL SULFONATES

CAS Number	ACUTE TOXICITY TO FISH 96-hr LL ₅₀ (mg/L) ¹	ACUTE TOXICITY TO INVERTEBRATES 48-hr EL ₅₀ (mg/L) ¹	TOXICITY TO ALGAE 96-hr EL ₅₀ (mg/L) ¹
	Available Data & Proposed Testing	Available Data & Proposed Testing	Available Data & Proposed Testing
115829-36-2	No testing needed Bridging	No testing needed Bridging	No testing needed Bridging
115733-09-0	Limit Test	>1,000 (WAF ³ , D)	>1,000 (WAF ³ , P, R) >1,000 (WAF ³ , P, B)
115733-10-3	No testing needed Bridging	No testing needed Bridging	No testing needed Bridging
68608-26-4	Limit Test	Limit Test	Limit Test
61789-86-4	Limit Test on T >10,000 (WAF ² , S)	Limit Test	Limit Test
68783-96-0	No testing needed Bridging	No testing needed Bridging	No testing needed Bridging
61790-48-5	Limit Test	No testing needed Bridging	No testing needed Bridging
78330-12-8	No testing needed Bridging	No testing needed Bridging	No testing needed Bridging

¹Toxicity endpoints are expressed as median lethal loading rates (LL₅₀) for fish and median effective loading rates (EL₅₀) for *Daphnia* and algae. The EL/LL₅₀ is defined as the loading rate that adversely effects 50% of the test organisms exposed to it during a specific time. The greater the EL/LL₅₀ the lower the toxicity.

²WAF = Water accommodated fraction static renewal test.

³WAF = Water accommodated fraction static non-renewal test.

⁴EL/LL₀ = no mortality or effects observed at the highest loading rate tested.

F = fathead minnow, *Pimephales promelas*.

D = freshwater cladoceran, *Daphnia magna*.

P = freshwater algae *Pseudokirchneriella subcapitata* formerly called *Selenastrum capricornutum*.

T = rainbow trout, *Oncorhynchus mykiss* formerly called *Salmo gairdneri*.

S = sheepshead minnow, *Cyprinodon variegatus*.

R = algae growth rate.

B = algae biomass.

**TABLE 6. EVALUATION OF AQUATIC TOXICOLOGY OF PETROLEUM ADDITIVE ALKARYL SULFONATES
(CONT.)**

CAS Number	ACUTE TOXICITY TO FISH 96-hr LL ₅₀ (mg/L)	ACUTE TOXICITY TO INVERTEBRATES 48-hr EL ₅₀ (mg/L) ¹	TOXICITY TO ALGAE 96-hr EL ₅₀ (mg/L)
	Available Data & Proposed Testing	Available Data & Proposed Testing	Available Data & Proposed Testing
71549-79-6	No testing needed Bridging	No testing needed Bridging	No testing needed Bridging
71486-79-5	>1,000 (WAF ² , F)	>1,000 (WAF ³ , D)	>1,000 (WAF ³ , P, R) >1,000 (WAF ³ , P, B)
70024-69-0	No testing needed Bridging	No testing needed Bridging	No testing needed Bridging
70024-71-4 C20-C24 analog of 70024-69-0	>10,000 (WAF ² , S)	No testing needed	No testing needed
71786-47-5	>1,000 (WAF ² , F) >10,000 (WAF ² , S)	>1,000 (WAF ³ , D)	>1,000 (WAF ³ , P, R) >1,000 (WAF ³ , P, B)

¹Toxicity endpoints are expressed as median lethal loading rates (LL₅₀) for fish and median effective loading rates (EL₅₀) for *Daphnia* and algae. The EL/LL₅₀ is defined as the loading rate that adversely effects 50% of the test organisms exposed to it during a specific time. The greater the EL/LL₅₀ the lower the toxicity.

²WAF = Water accommodated fraction static renewal test.

³WAF = Water accommodated fraction static non-renewal test

⁴EL/LL₀ = no mortality or effects observed at the highest loading rate tested.

F = fathead minnow, *Pimephalespromelas*.

D = freshwater cladoceran, *Daphnia magna*.

P = freshwater algae *Pseudokirchneriella subcapitata* formerly called *Selenastrum capricornutum*.

T = rainbow trout, *Oncorhynchus mykiss* formerly called *Salmo gairdneri*.

S = sheepshead minnow, *Cyprinodon variegatus*.

R = algae growth rate.

B = algae biomass.

TABLE 7. EVALUATION OF ACUTE MAMMALIAN TOXICOLOGY OF PETROLEUM ADDITIVE ALKARYL SULFONATES

CAS Number	ACUTE ORAL TOXICITY ¹	ACUTE DERMAL TOXICITY ¹	ACUTE INHALATION TOXICITY ¹
	Available Data & Proposed Testing	Available Data & Proposed Testing	Available Data & Proposed Testing
115829-3 6-2	No testing needed Bridging	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
115733-09-O	LD ₅₀ > 5.0 g/kg (rat)	LD ₅₀ > 5.0 g/kg (rabbit)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
115733-10-3	No testing needed Bridging	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
68608-26-4	LD ₅₀ > 5.0 g/kg (rat)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
6 1789-86-4	LD ₅₀ > 5.0 g/kg (rat)	LD ₅₀ > 5.0 g/kg (rabbit)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
68783-96-O	LD ₅₀ > 5.0 g/kg (rat)	LD ₅₀ > 2.0 g/kg (rabbit)	² LC ₀ = 1.9 mg/L (rat)
61790-48-5	LD ₅₀ > 2.0 g/kg (rat)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
78330-12-8	LD ₅₀ > 5.0 g/kg (rat)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
7 1549-79-6	LD ₅₀ = 14.9g/kg (rat)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results

¹Toxicity endpoints are expressed as median lethal dose (LD₅₀) for acute oral and dermal toxicity and median lethal concentration (LC₅₀) for acute inhalation toxicity. The LD/LC₅₀ is defined as the dose/concentration that is lethal to 50% of the test organisms. The greater the LD/LC₅₀, the lower the toxicity.

²LC₀ = no mortality observed at the highest concentration tested.

TABLE 7. EVALUATION OF ACUTE MAMMALIAN TOXICOLOGY OF PETROLEUM ADDITIVE ALKARYL SULFONATES (CONT.)

CAS Number	ACUTE ORAL TOXICITY ¹	ACUTE DERMAL TOXICITY ¹	ACUTE INHALATION TOXICITY ¹
	Available Data & Proposed Testing	Available Data & Proposed Testing	Available Data & Proposed Testing
71486-79-8	No testing needed Bridging	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
-70024-69-o	No testing needed Bridging	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
C20-C24 alkaryl calcium salt (no CAS #) analog of 70024-69-o	LD ₅₀ > 5.0 g/kg (rat)	LD ₅₀ > 5.0 g/kg (rat)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results
7 178647-5	LD ₅₀ > 16.0 g/kg (rat)	No testing needed Acute toxicity end point satisfied by acute oral toxicity results	No testing needed Acute toxicity end point satisfied by acute oral toxicity results

¹Toxicity endpoints are expressed as median lethal dose (LD₅₀) for acute oral and dermal toxicity and median lethal concentration (LC₅₀) for acute inhalation toxicity. The LD/LC₅₀ is defined as the dose/concentration that is lethal to 50% of the test organisms. The greater the LD/LC₅₀, the lower the toxicity.

²LC₀ = no mortality observed at the highest concentration tested.

TABLE 8. EVALUATION OF MUTAGENICITY OF PETROLEUM ADDITIVE ALKARYL SULFONATES

CAS Number	GENE MUTATION ASSAY	CHROMOSOMAL ABERRATION ASSAY
	Available Data & Proposed Testing	Available Data & Proposed Testing
115829-3 6-2	No testing needed Bridging	No testing needed Bridging
115733-09-0	No testing needed Bridging	No testing needed Bridging
115733-1 o-3	No testing needed Bridging	No testing needed Bridging
68608-26-4	No testing needed Bridging	No testing needed Bridging
6 1789-86-4	No testing needed Bridging	No testing needed Bridging
68783-96-0	Bacterial Reverse Mutation Assay — Not mutagenic Mouse Lymphoma Mutagenicity Screen Not mutagenic	Mouse Micronucleus Assay — Not clastogenic In <i>vitro</i> CHO Cell Chromosomal Aberration Assay — Not clastogenic
6 1790-48-5	No testing needed Bridging	No testing needed Bridging
C15-C21 alkaryl sodium salt (no CAS #) analog of 78330-12-8	Bacterial Reverse Mutation Assay Not mutagenic	No testing needed Bridging
78330-12-g	No testing needed Bridging	No testing needed Bridging
7 1549-79-6	No testing needed Bridging	No testing needed Bridging
7 1486-79-8	No testing needed Bridging	No testing needed Bridging

TABLE 8. EVALUATION OF MUTAGENICITY OF PETROLEUM ADDITIVE ALKARYL SULFONATES (CONT.)

CAS Number	GENE MUTATION ASSAY	CHROMOSOMAL ABERRATION ASSAY
	Available Data & Proposed Testing	Available Data & Proposed Testing
70024-69-O	No testing needed Bridging	No testing needed Bridging
C20-C24 alkaryl calcium salt (no CAS #) analog of 70024-69-o	Bacterial Reverse Mutation Assay — Not mutagenic	Mouse Micronucleus Assay — Not clastogenic
7 1786-47-5	Bacterial Reverse Mutation Assay — Not mutagenic	Mouse Micronucleus Assay — Not clastogenic <i>In vitro</i> CHO Cell Chromosomal Aberration Assay — Not clastogenic

**TABLE 9. EVALUATION OF REPEATED-DOSE MAMMALIAN TOXICOLOGY OF PETROLEUM ADDITIVE
ALKARYL SULFONATES**

CAS Number	REPEATED-DOSE TOXICITY	REPRODUCTIVE/DEVELOPMENTAL TOXICITY
	Available Data & Proposed Testing	Available Data & Proposed Testing
115829-36-2	No testing needed Bridging	No testing needed Bridging
115733-09-0	Test	Test
115733-10-3	No testing needed Bridging	No testing needed Bridging
68608-26-4	No testing needed Bridging	No testing needed Bridging
6 1789-86-4	No testing needed Bridging	No testing needed Bridging
68783-96-0	<p>2%-day repeated-dose dermal study in rats (OECD 410) NOAEL = 1000 mg/kg/day (highest dose tested)</p> <p>28-day inhalation study in rats (OECD 412) NOAEL = 49.5 mg/m³ At 260 mg/m³,</p> <ul style="list-style-type: none"> • signs of toxicity, • decreased body weight gain (males), • increased lung weights, • intraalveolar microphage accumulation, • bronchiole epithelium hyperplasia/hypertrophy; <p>At 156 mg/m³,</p> <ul style="list-style-type: none"> • signs of toxicity, • increased lung weights, • intra-alveolar microphage accumulation, • bronchiole epithelium hyperplasia/hypertrophy; <p>At 49.5 mg/m³,</p> <ul style="list-style-type: none"> • no significant effects. 	No testing needed Bridging

**TABLE 9. EVALUATION OF REPEATED-DOSE MAMMALIAN TOXICOLOGY OF PETROLEUM ADDITIVE
ALKARYL SULFONATES (CONT.)**

CAS Number	REPEATED-DOSE TOXICITY	REPRODUCTIVE/DEVELOPMENTAL TOXICITY
	Available Data & Proposed Testing	Available Data & Proposed Testing
61790-48-5	No testing needed Bridging	No testing needed Bridging
78330-12-g	No testing needed Bridging	No testing needed Bridging
7 1549-79-6	No testing needed Bridging	No testing needed Bridging
71486-79-8	No testing needed Bridging	No testing needed Bridging
70024-69-o	No testing needed Bridging	No testing needed Bridging
C20-C24 alkaryl calcium salt (no CAS #) analog of 70024-69-O	4-week repeated-dose oral study in rats (OECD 407) NOAEL = 500 mg/kg/day At 1000 <u>mg/kg/day</u> , • decreased serum cholesterol; At 500 <u>mg/kg/day</u> , • no significant effects; At 100 <u>mg/kg/day</u> , • no significant effects.	No testing needed Bridging

**TABLE 9. EVALUATION OF REPEATED-DOSE MAMMALIAN TOXICOLOGY OF PETROLEUM ADDITIVE
ALKARYL SULFONATES (CONT.)**

CAS Number	REPEATED-DOSE TOXICITY	REPRODUCTIVE/DEVELOPMENTAL TOXICITY
	Available Data & Proposed Testing	Available Data & Proposed Testing
71786-47-5	<p>28-day repeated dose dermal study in rats (OECD 410) NOAEL = 1000 mg/kg/day (highest dose tested).</p> <p>2%day repeated dose dermal study in rabbits (OECD 410) <u>At 2.0 ml/kg/day.</u></p> <ul style="list-style-type: none"> · two males sacrificed in moribund condition; · decreased mean body weight; · alopecia and erythema, edema, atonia, desquamation, fissuring, and exfoliation of the skin; · decreased total leukocyte count; · decreased red blood cell count, hemoglobin, and hematocrit,(females only); · decreased total serum protein and serum globulin; · increased SGOT and serum alkaline phosphatase (males); · increased SGOT and SGPT (females); · increased liver weights and focal hepatocellular degeneration, necrosis, and vacuolation; · decreased testes weights with aspermatogenesis, decreased number of spermatids and diffuse tubular hypoplasia; • decreased epididymides weights with epithelial hypoplasia; <p><u>At 0.5 ml/kg/day.</u></p> <ul style="list-style-type: none"> · alopecia and erythema, edema, atonia, desquamation, fissuring, and exfoliation of the skin; · decreased total leukocyte count; · decreased total serum protein and serum globulin; · increased SGOT and serum alkaline phosphatase (males); · increased SGOT and SGPT (females); · increased liver weights; • decreased testes and epididymides weights. 	<p>No testing needed Bridging</p>